

EXHIBIT A

Filed: December 4, 2001 Express Mail: EL603009481US

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The Patent and Trademark Office stamping
sets forth and receipt date (or both the receipt date and the Serial Number) of a
continuation patent application identified as follows:

APPLICANT: Danishefsky, et al.

TITLE: Synthesis of Epothilones, Intermediates Thereof, Analogues and Uses
Thereof

Application Comprising: 112 pages (including 87 pages of description, 24 pages of
claims, and 1 page of Abstract);
and 59 sheets of drawings;

Using: Utility Patent Application Transmittal (5 pp.);
Fee Transmittal (1 pg., 2 copies); Preliminary Amendment (11 pp.);
Identification of Patent Under 37 CFR §1.607(c) (1 pg.); Statement Filed Pursuant to
Duty of Disclosure Under 37 CFR §§1.56, 1.97 and 1.98 (3 pp.); Form PTO-1449
Information Disclosure Statement (3 pp.); Copy of Executed and Recorded
Assignments (12 pp. total); Copy of Notice Regarding Power of Attorney (1 pg.);
Copy of Executed Declaration Claiming Small Entity Status -Nonprofit
Organization (2 pp.); Copy of Executed Declarations (8 pp. total); ~~Copy of Formal
Drawings (76 Sheets)~~ Return Postcard.

Check in the amount of \$370.00 for Basic Filing Fee (Small Entity)
Authorization to charge additional fees to Deposit Account No. 03-1721

Attorney: KKS
3341830_1.DOC

Case No. 2003080-0071 (SK-744-CON4)



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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
08/986,025 <i>2003080-0037</i>	12/03/1997	SAMUEL J. DANISHEFSKY	1078/1C598US

KAROLINE K. M. SHAIR
CHOATE, HALL & STEWART
EXCHANGE PLACE, 53 STATE STREET
BOSTON, MA 02109

Date Mailed: 04/17/2000

NOTICE REGARDING POWER OF ATTORNEY

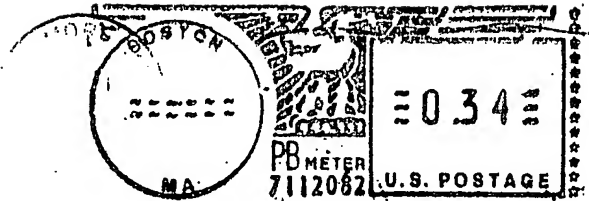
This is in response to the Power of Attorney filed 03/27/2000.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

Legend Harmon / Brenda Gay

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Initial Patent Examination Division (703) 308-1202

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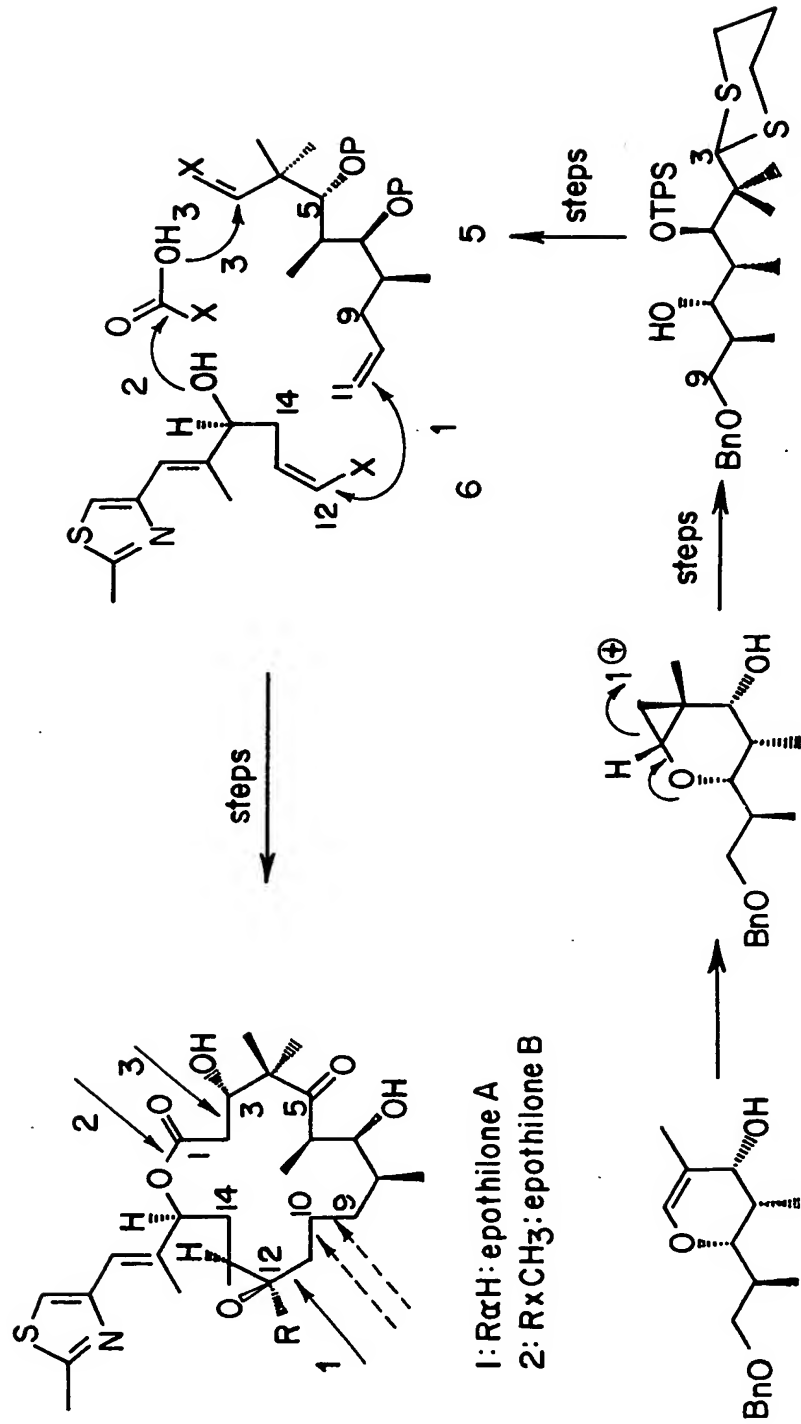
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FIG. 1A



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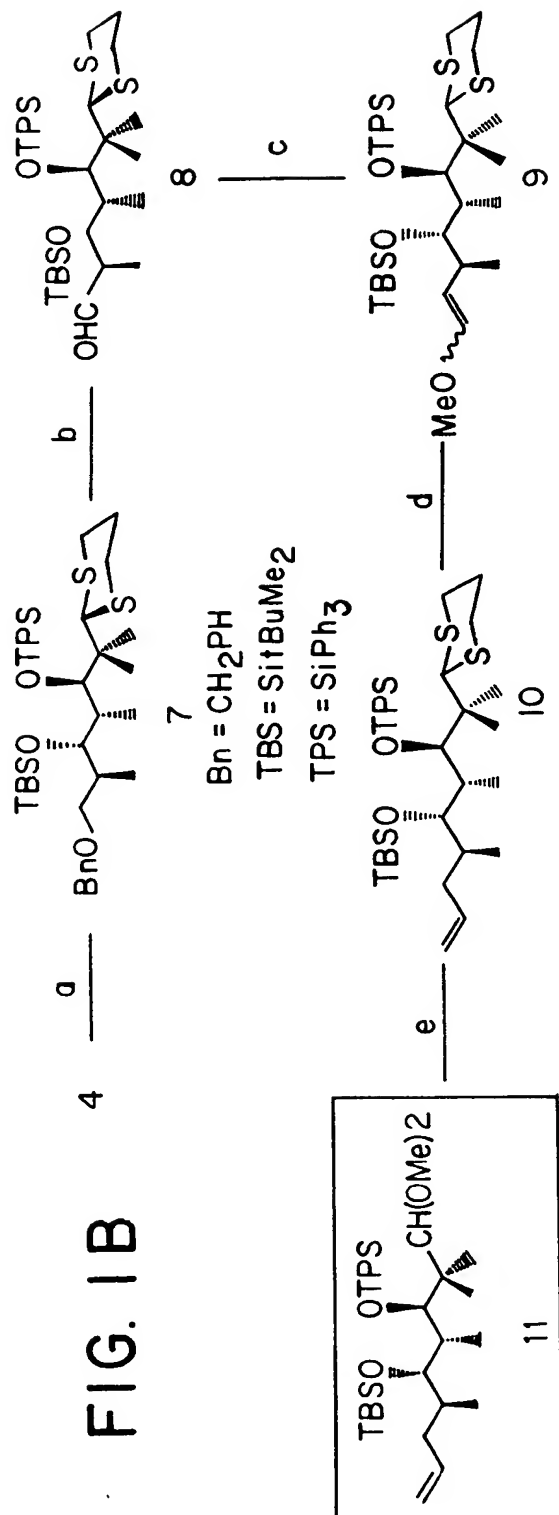


FIG. 12A

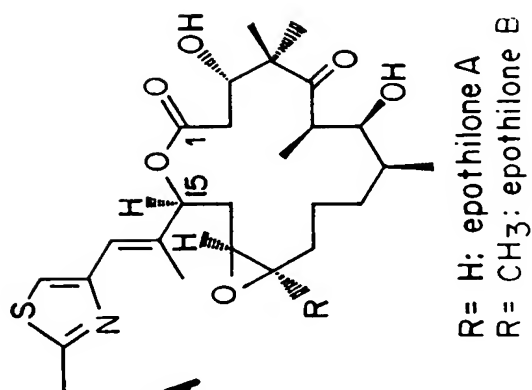
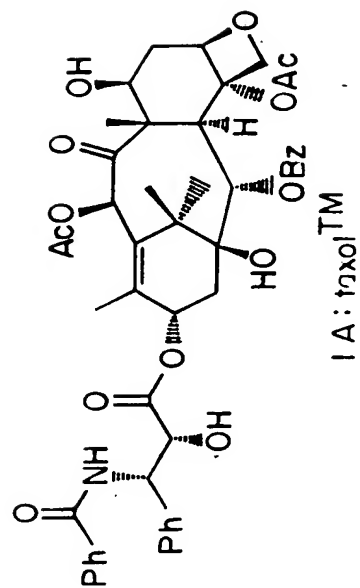


FIG. 12B



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FIG. 2

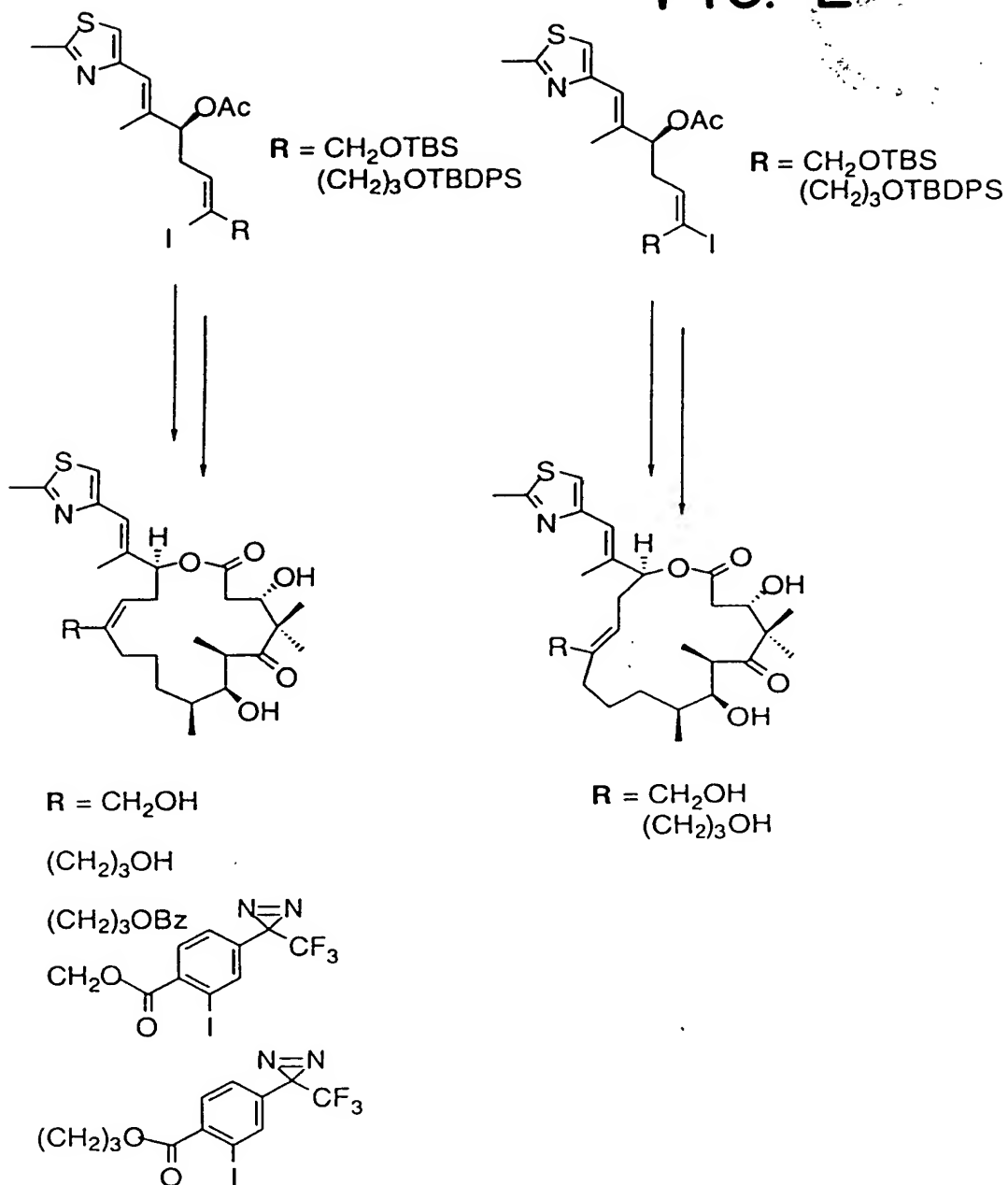




FIG. 3B

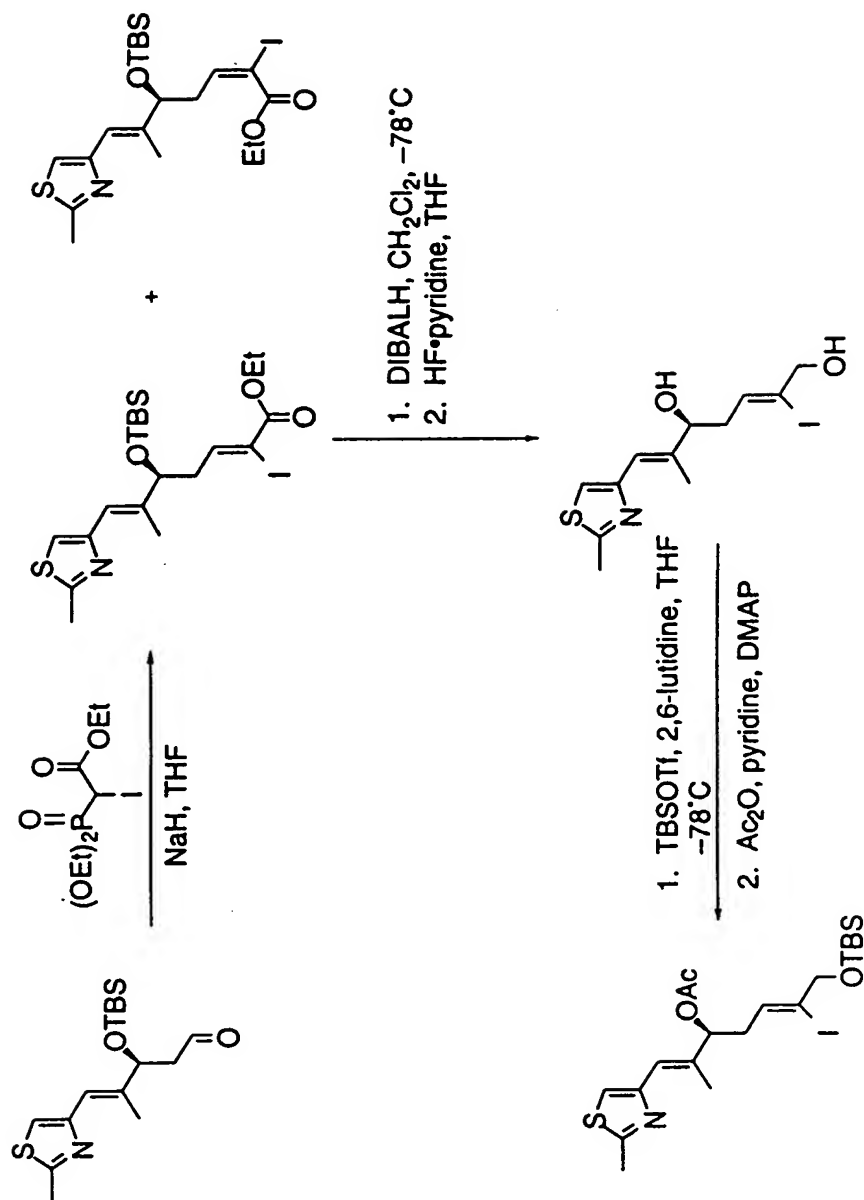
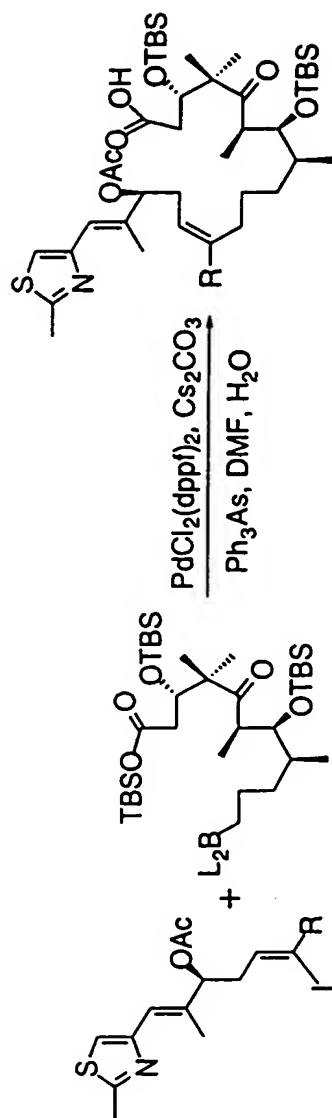


FIG. 3C



$R = CH_2OTBS$
 $(CH_2)_3OTBDPS$

K_2CO_3
 $MeOH, H_2O$

A ——— A

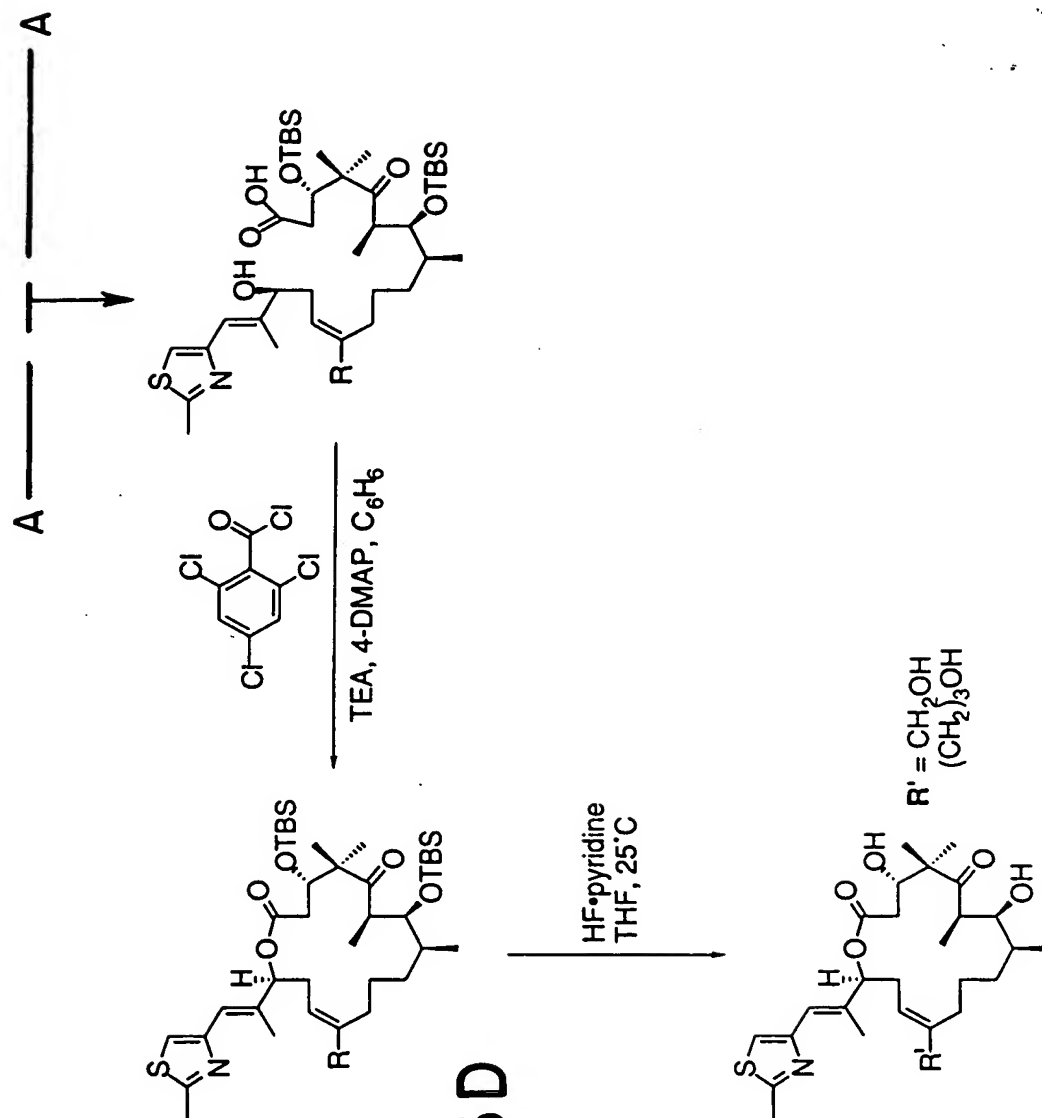


FIG. 3D

FIG. 3E

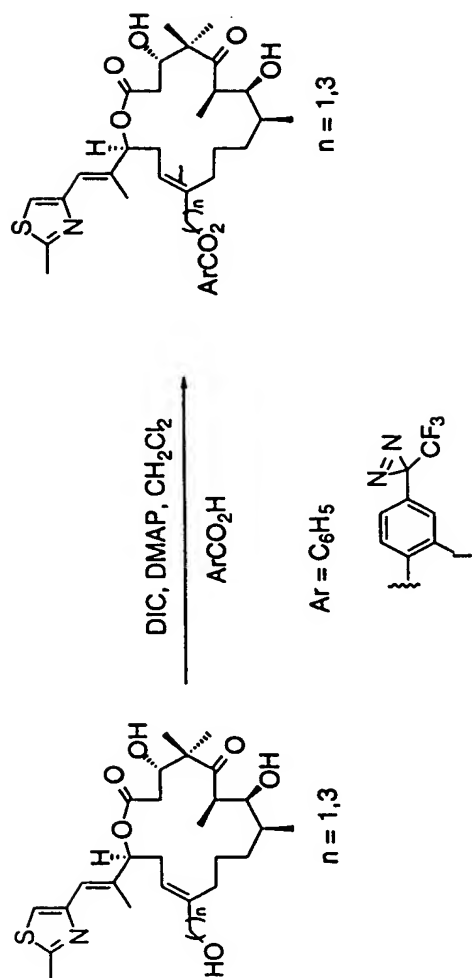


FIG. 3F

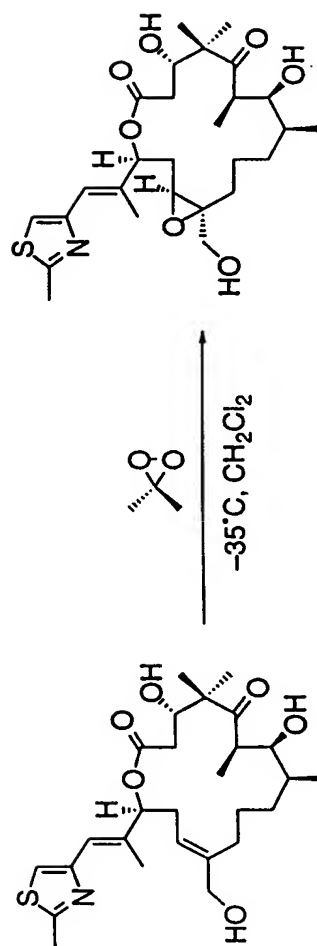


FIG. 4A

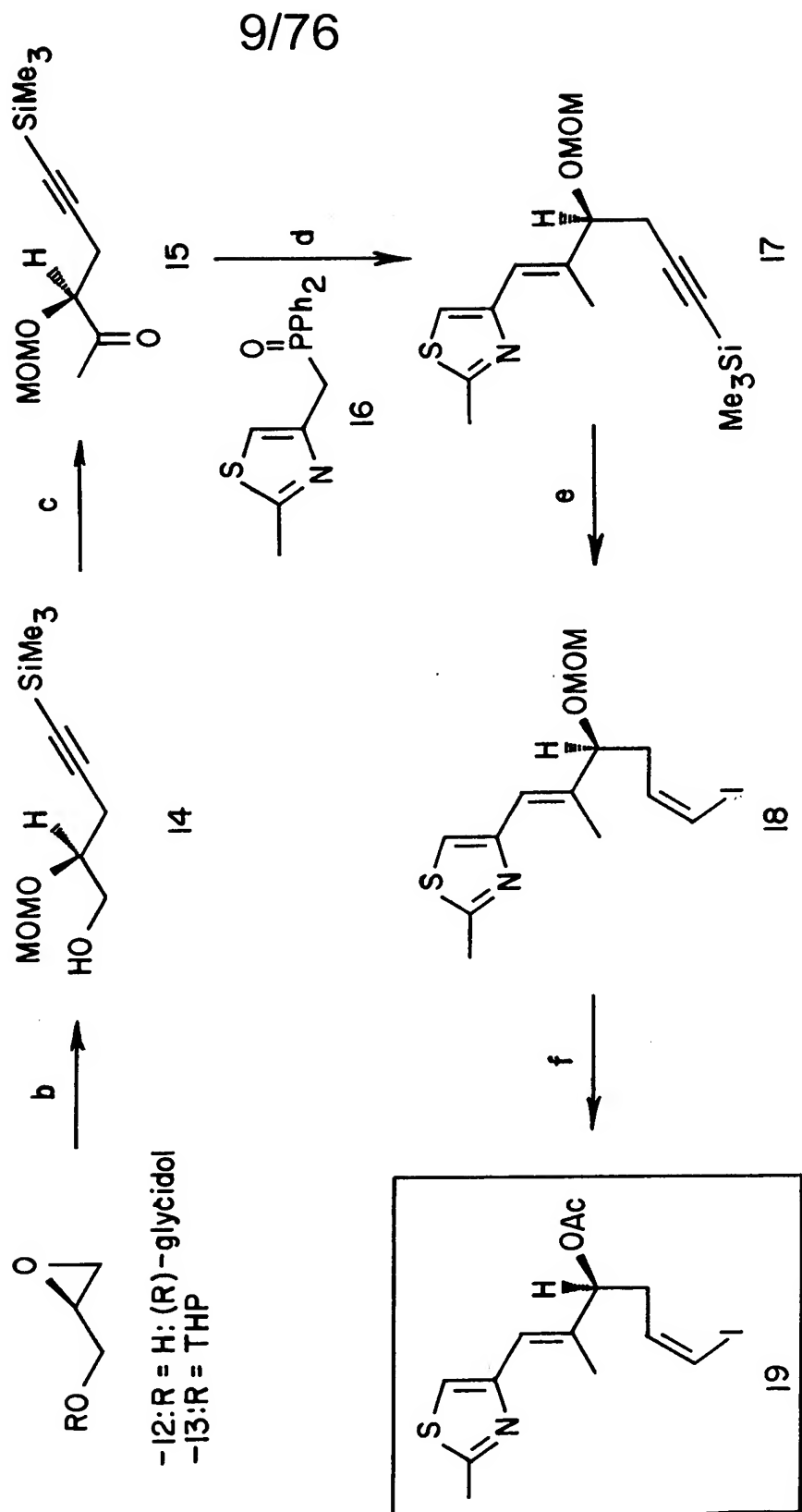


FIG. 4A

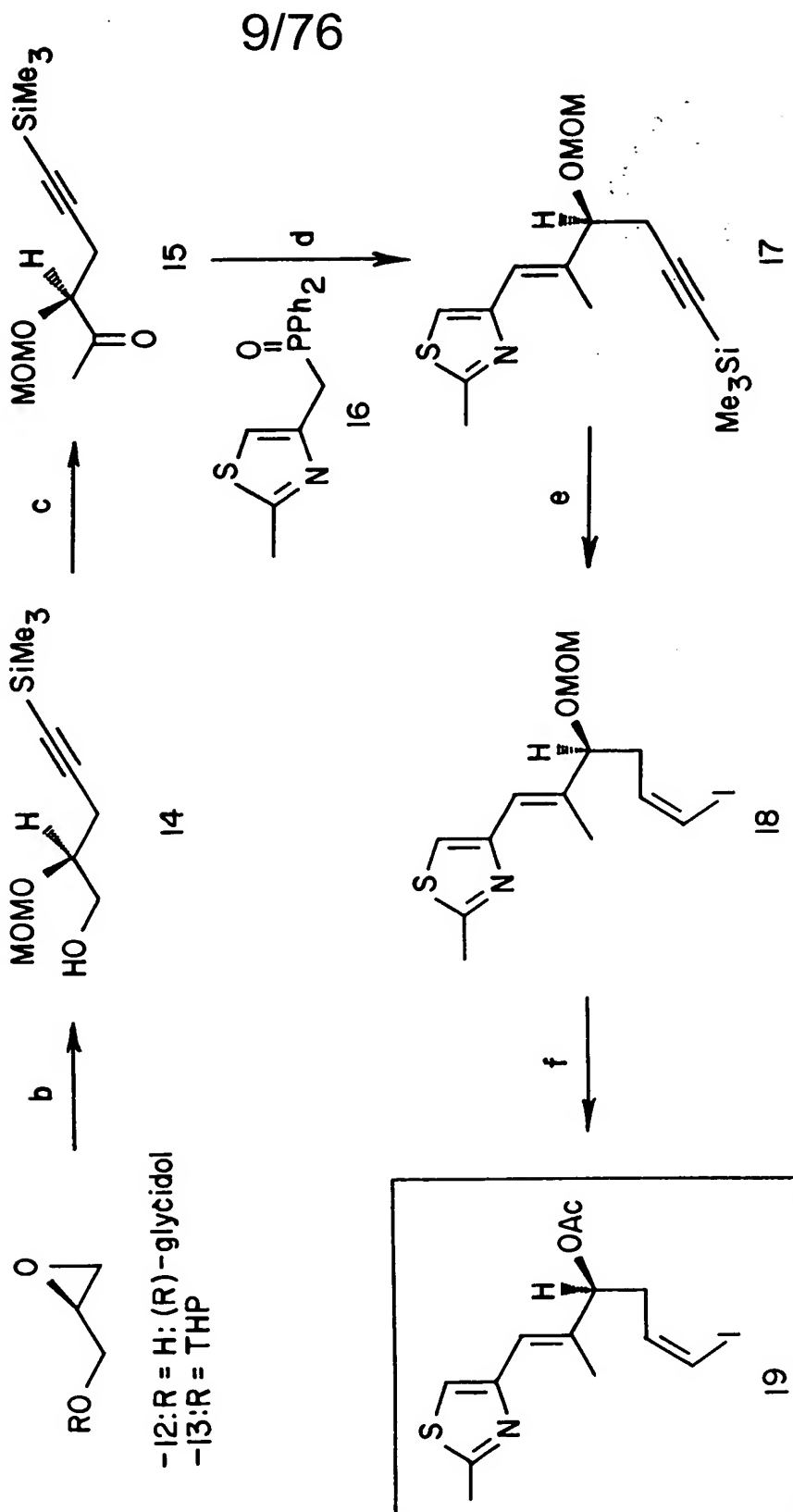
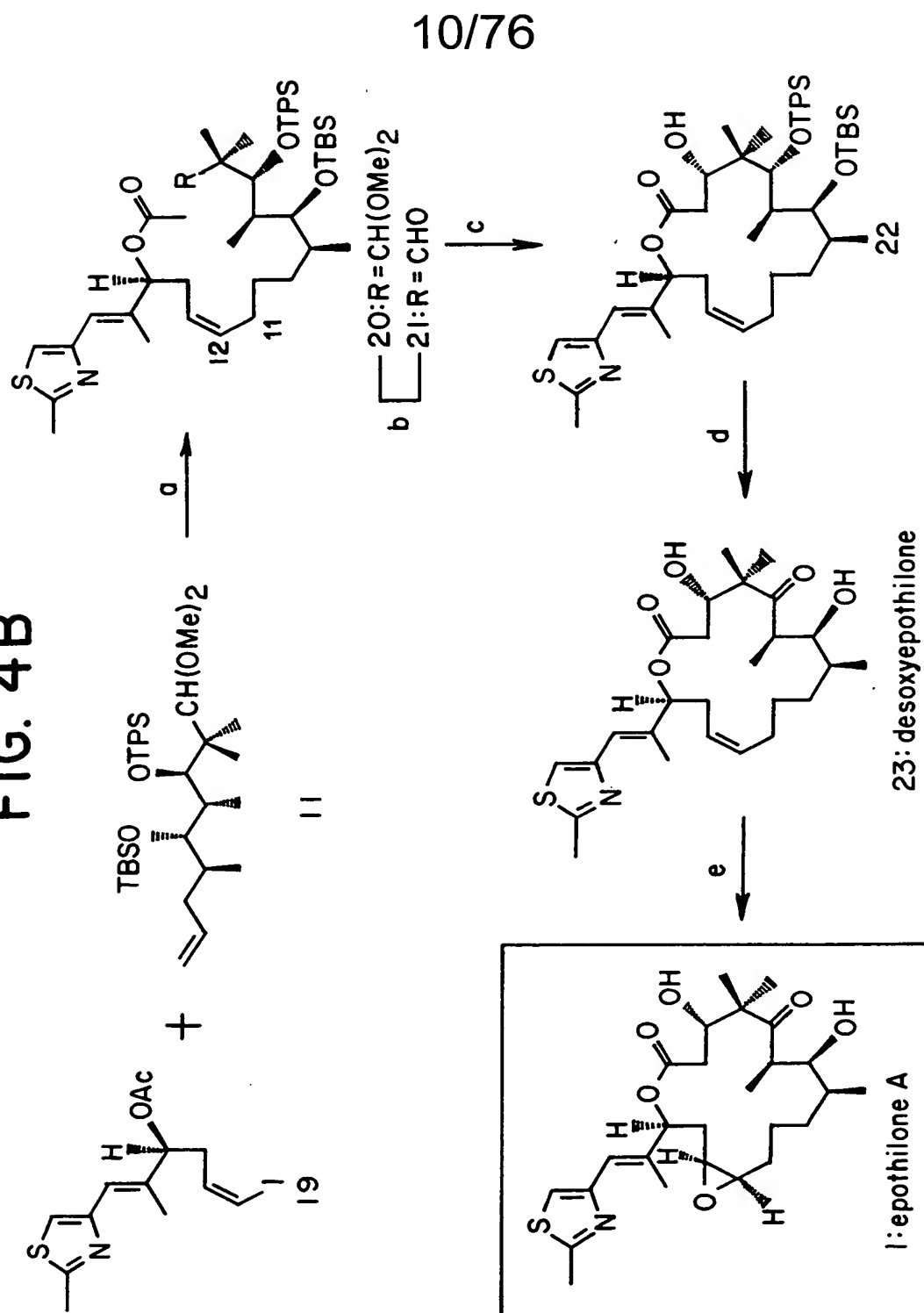
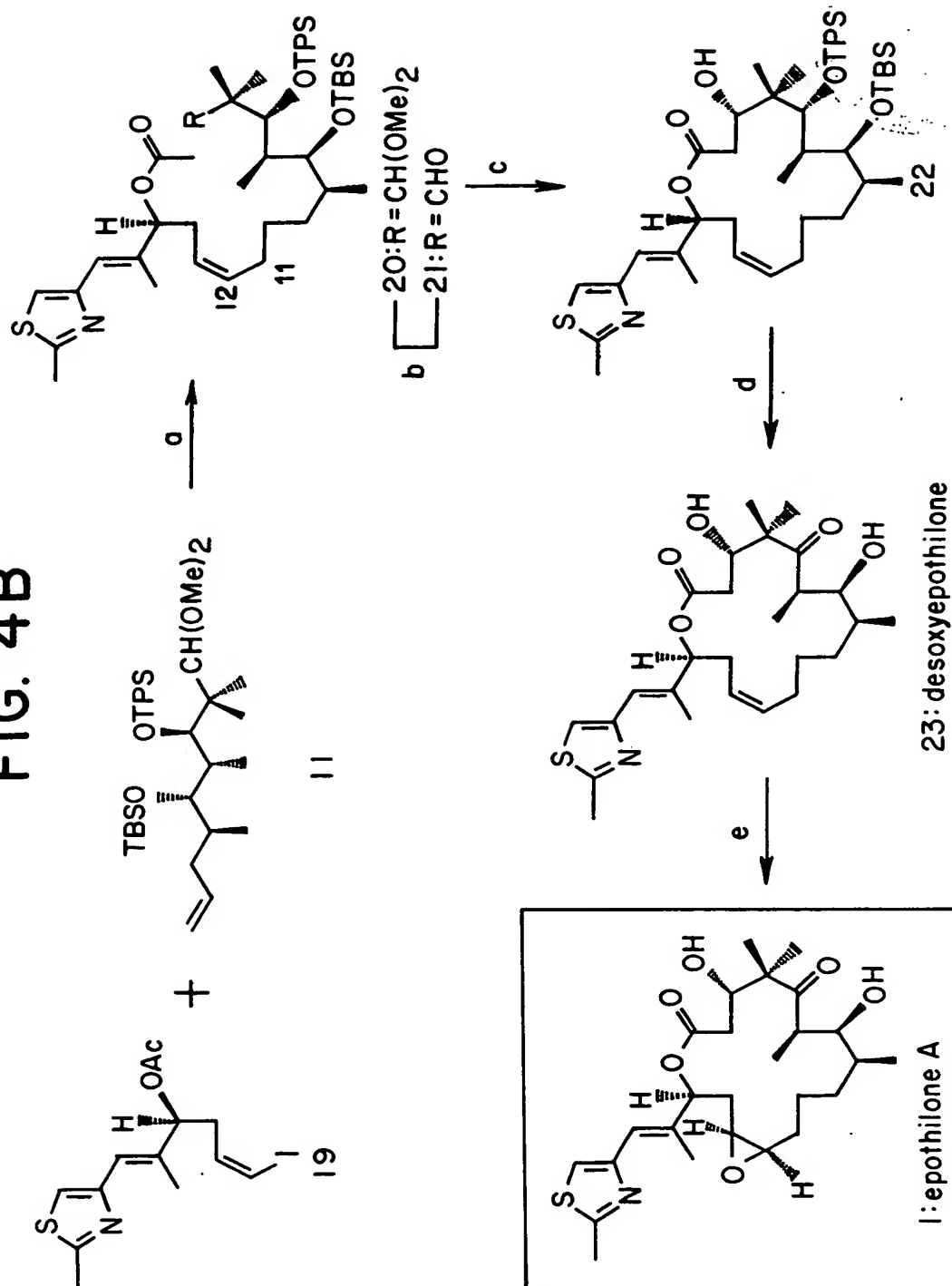


FIG. 4B



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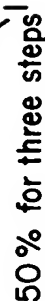


FIG. 6A

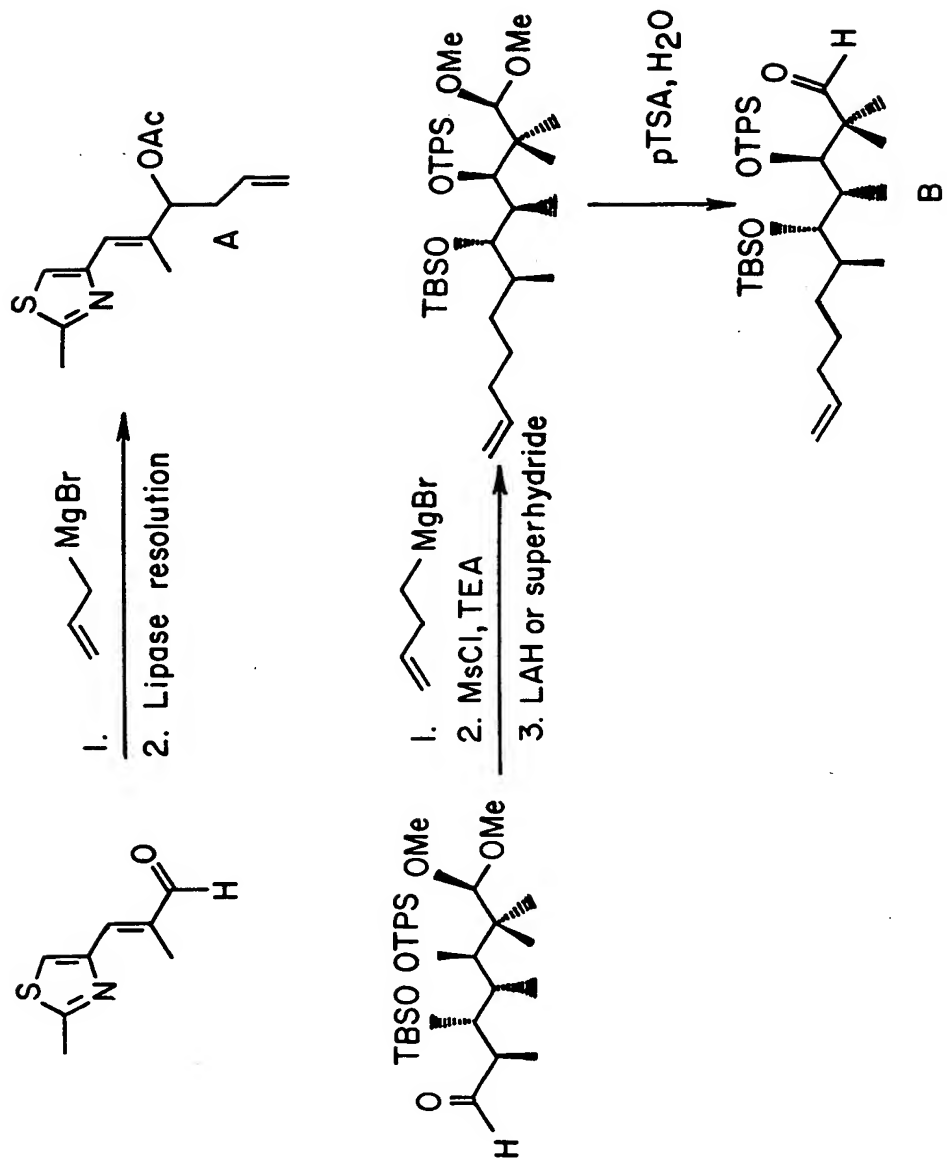
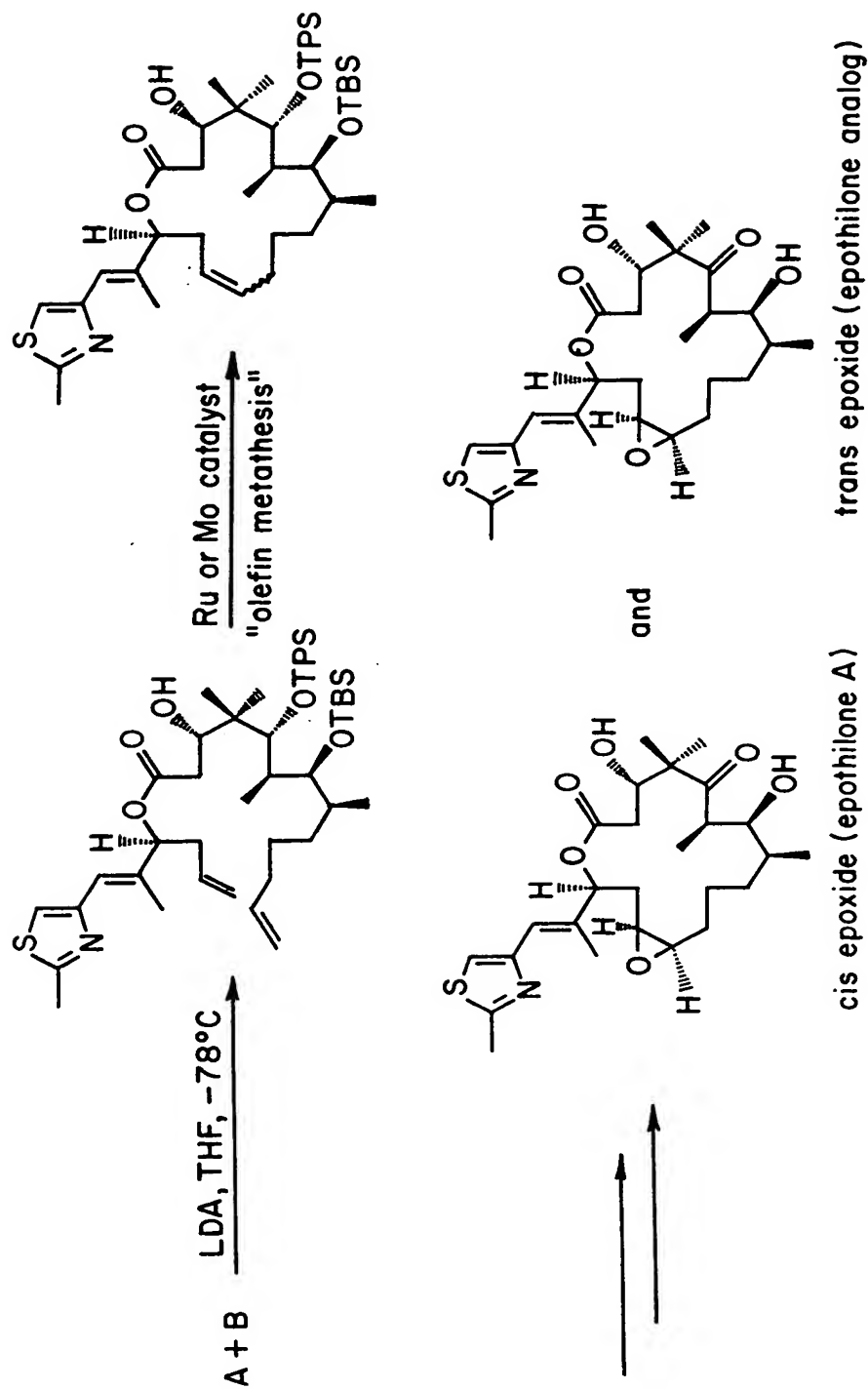
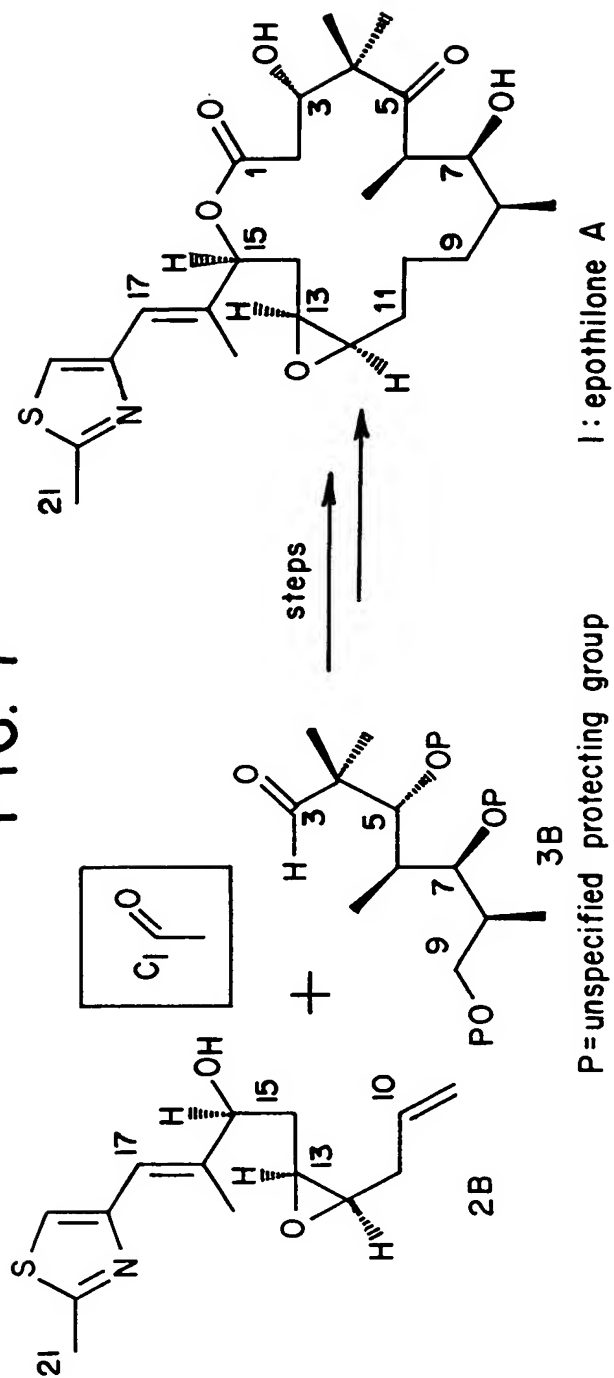


FIG. 6B

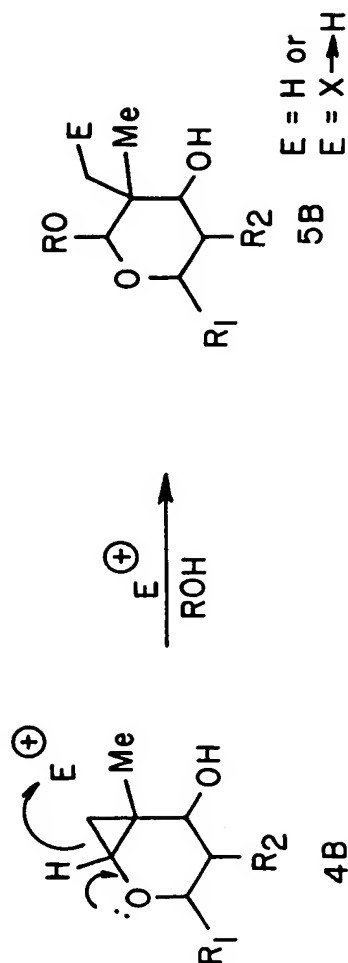


*17 steps from known starting materials vs. 27 steps for aldol macrocyclization

FIG. 7



Convergent strategy for a total synthesis of epothilone A (1).



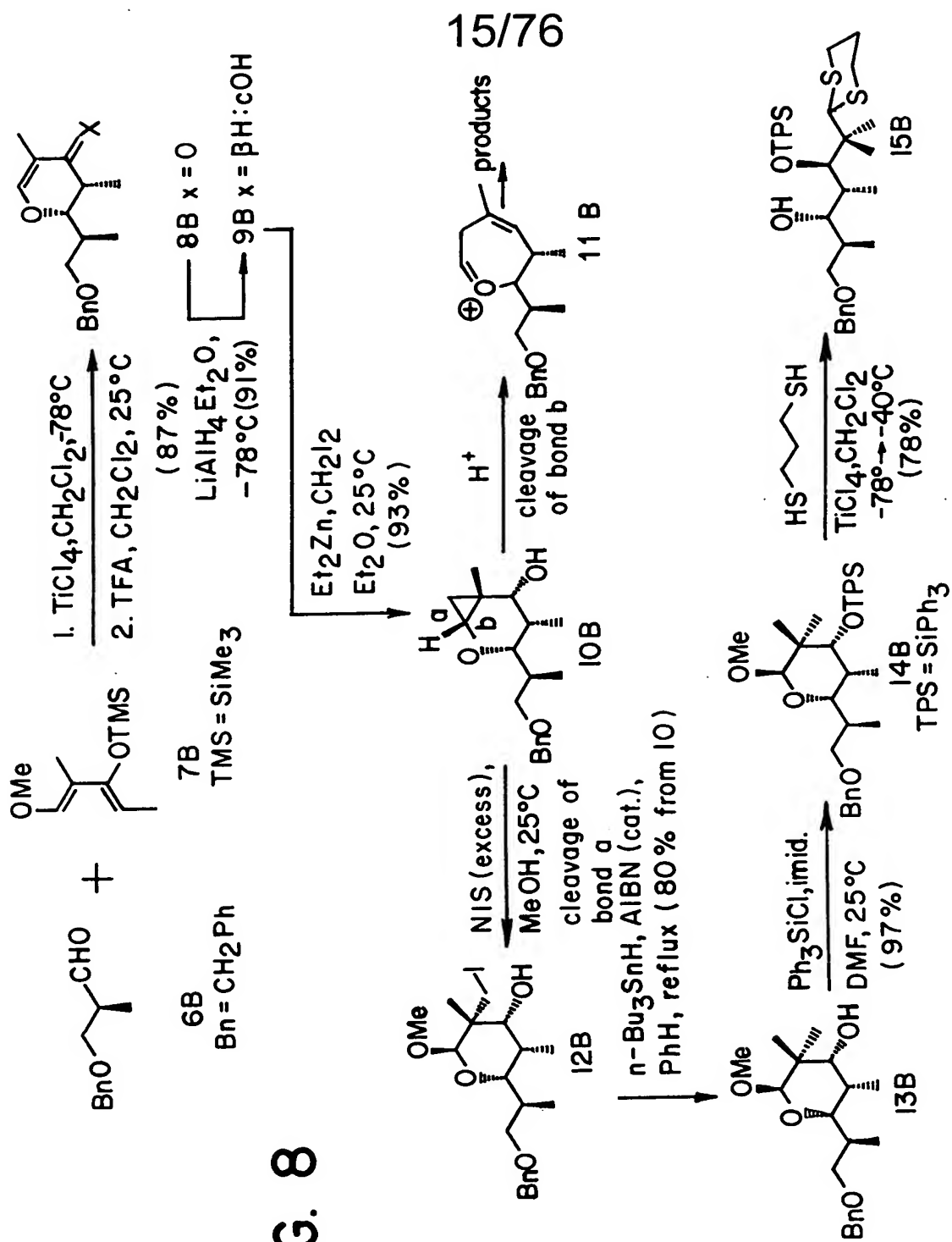
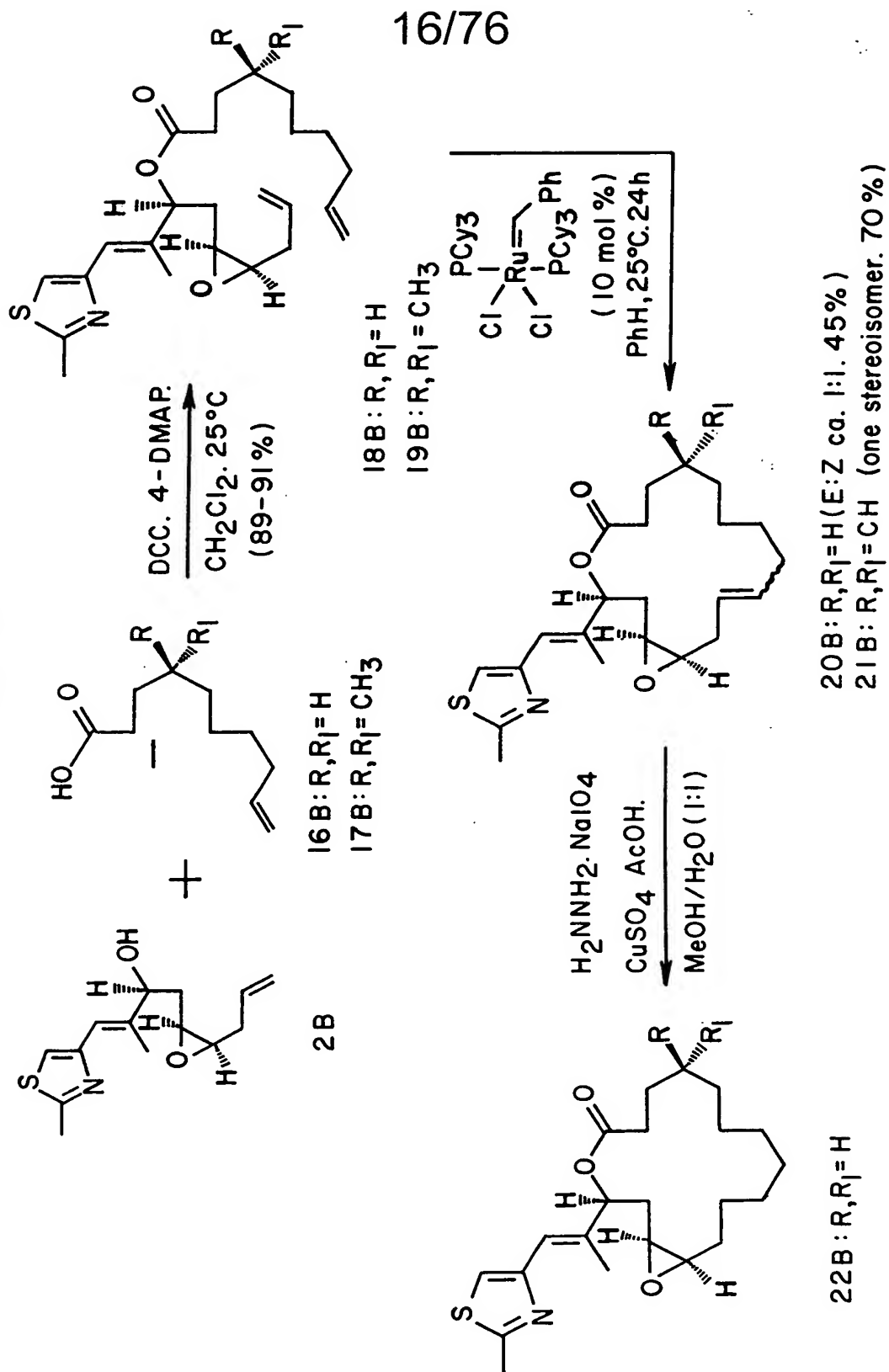


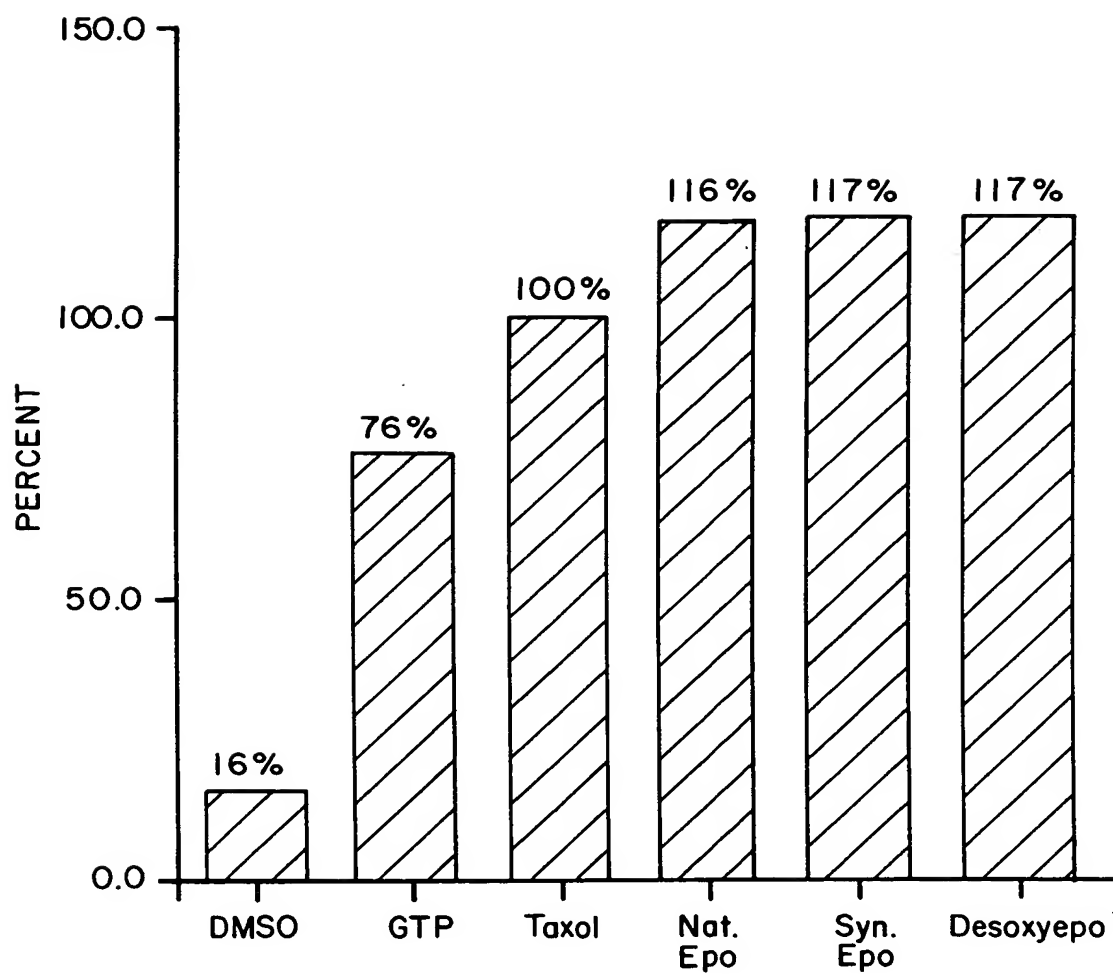
FIG. 8

FIG. 9



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FIG. 10



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FIG. II

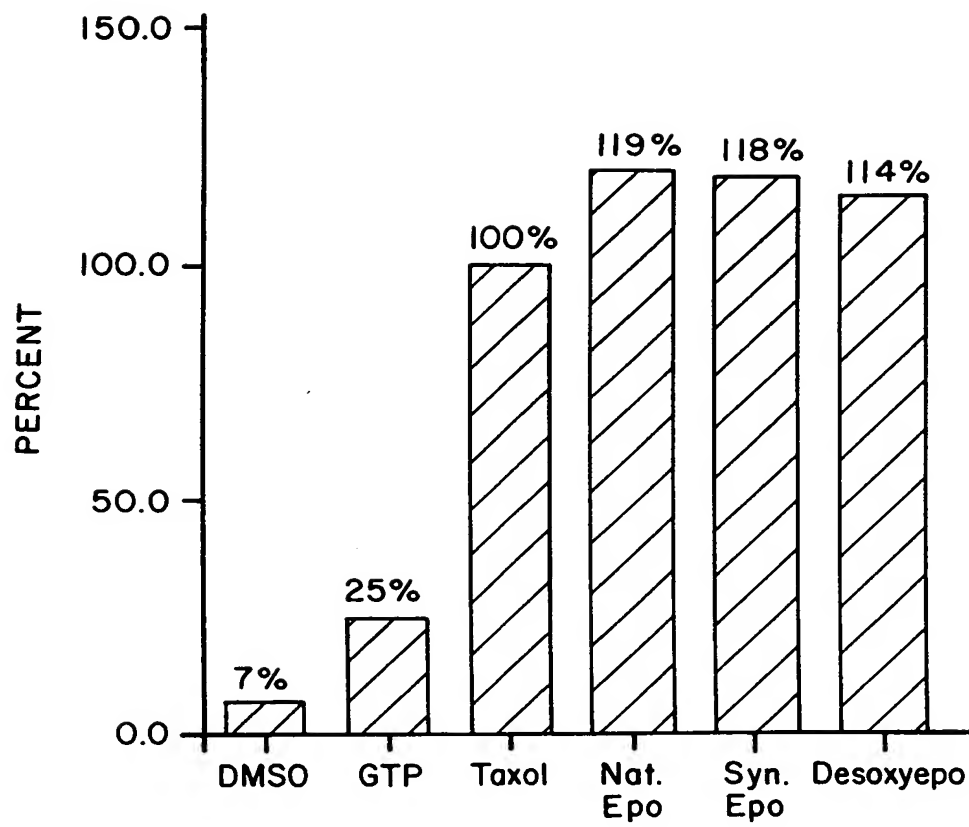


FIG. 13

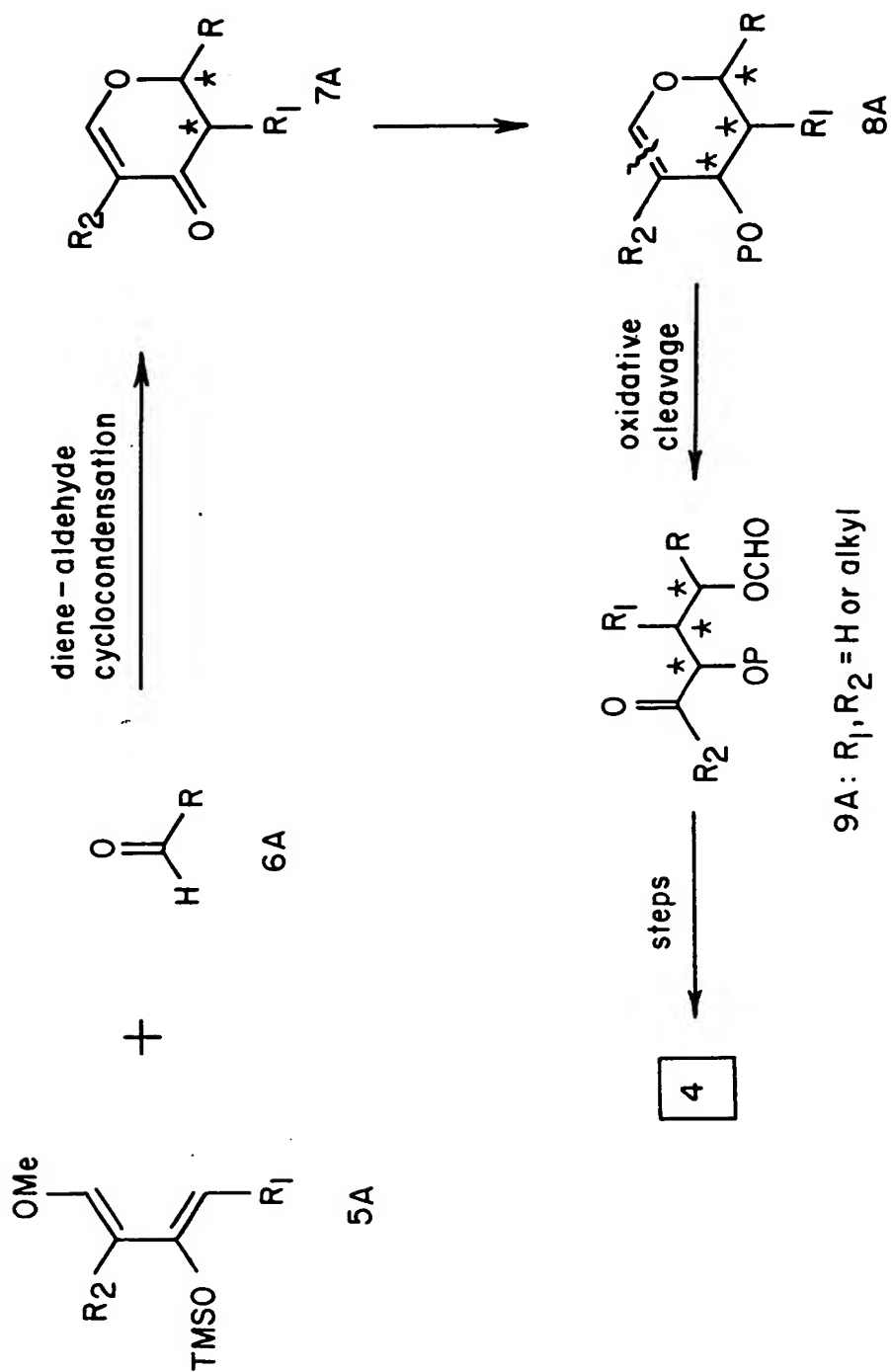


FIG. 14A

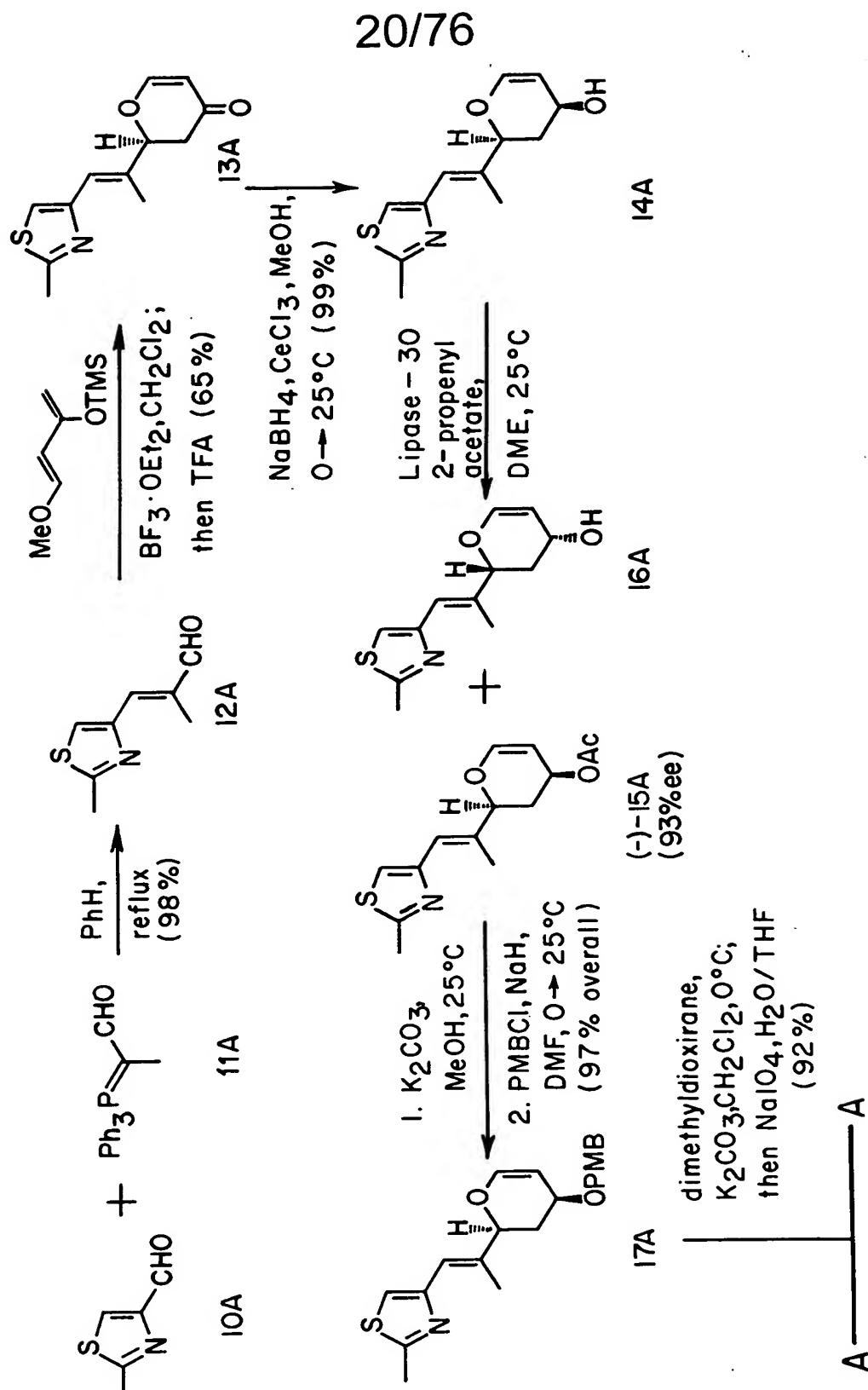


FIG. 14B

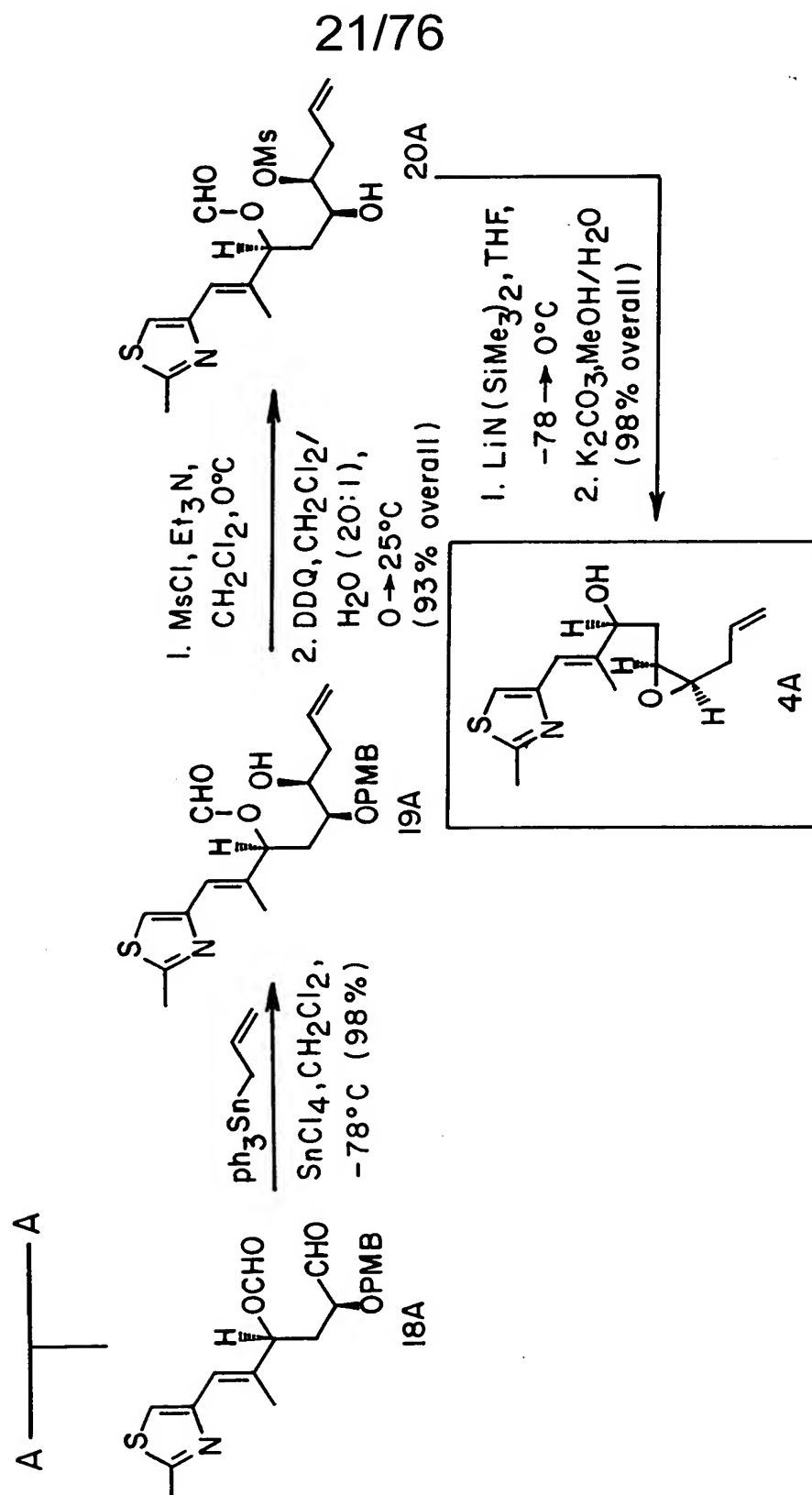


FIG. 15

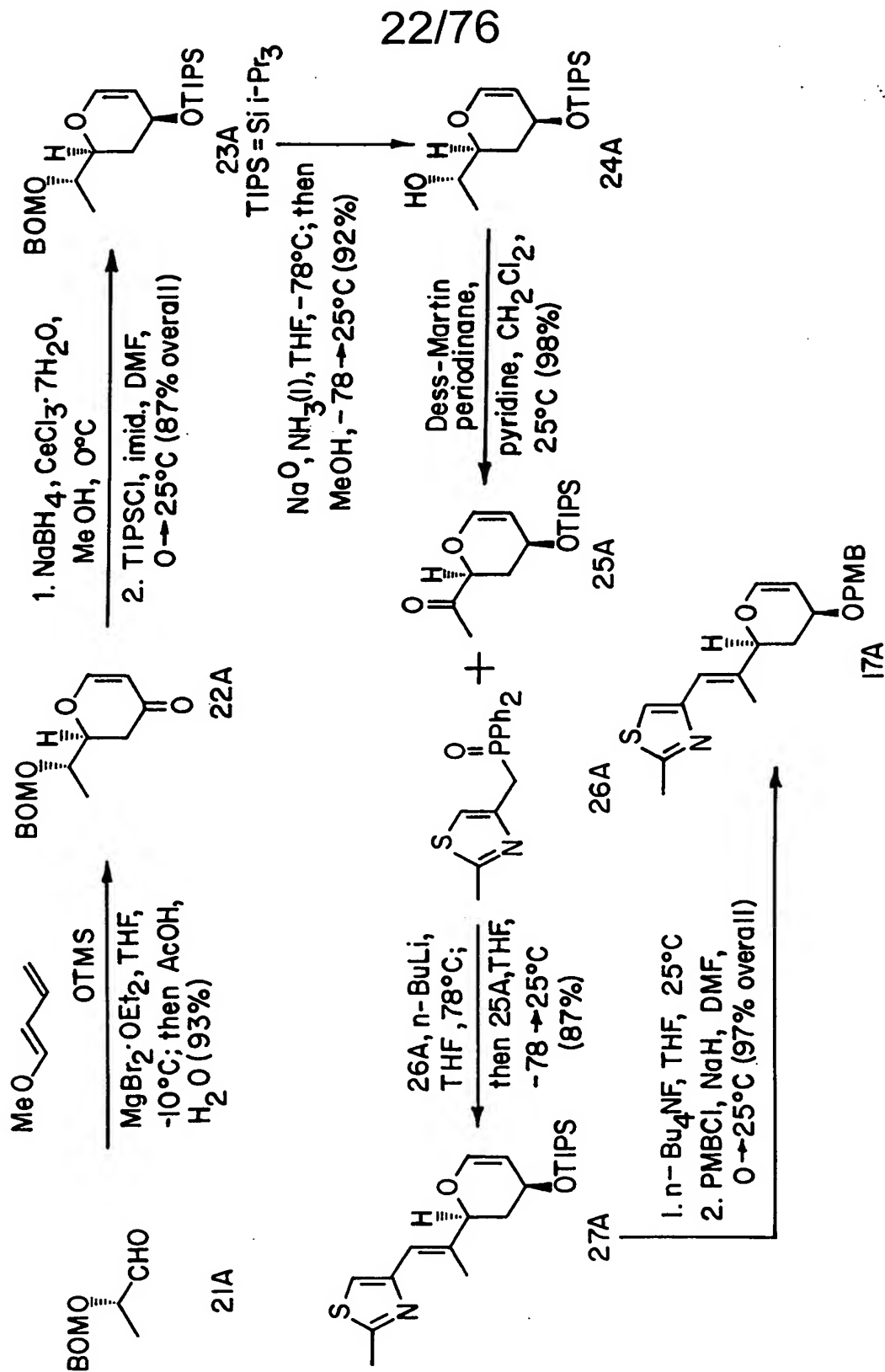


Fig. 16

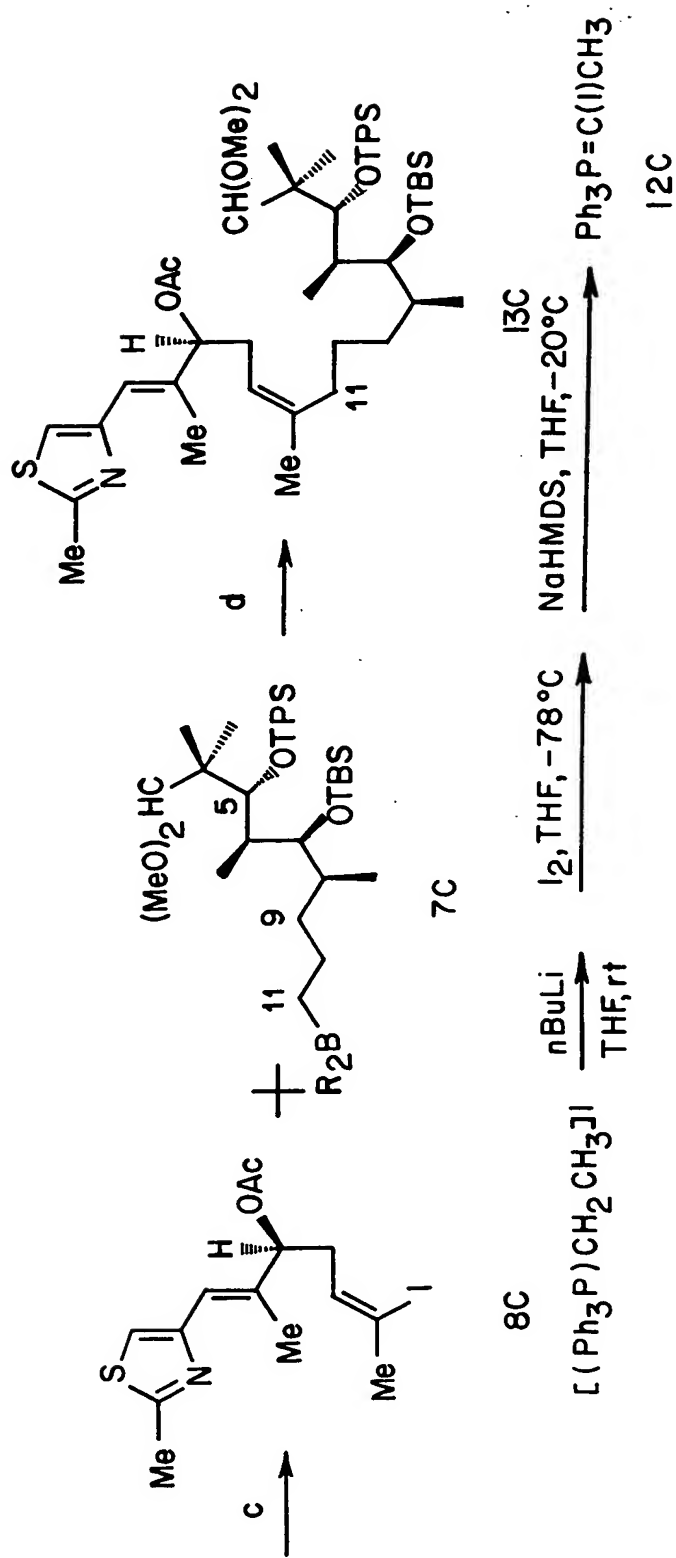
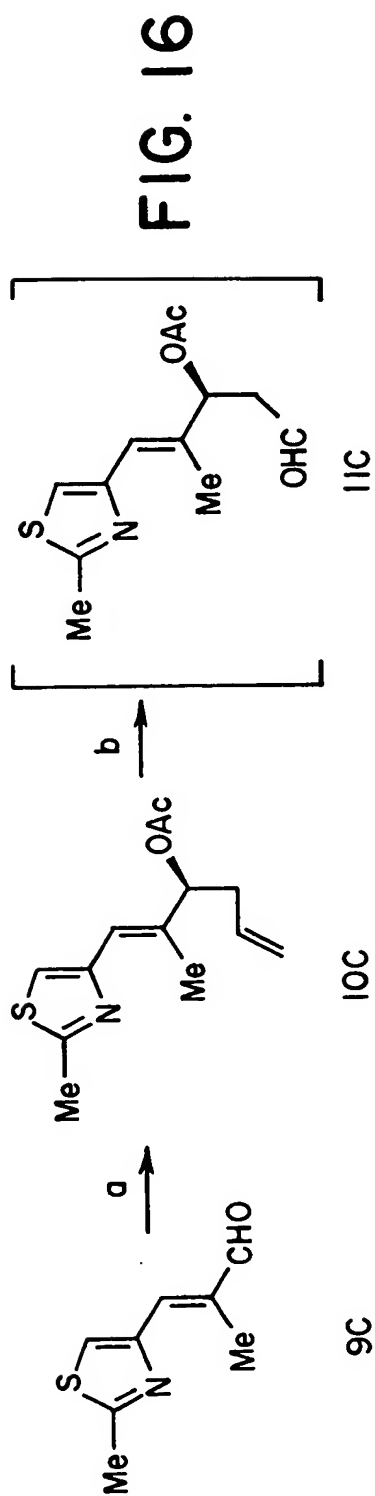
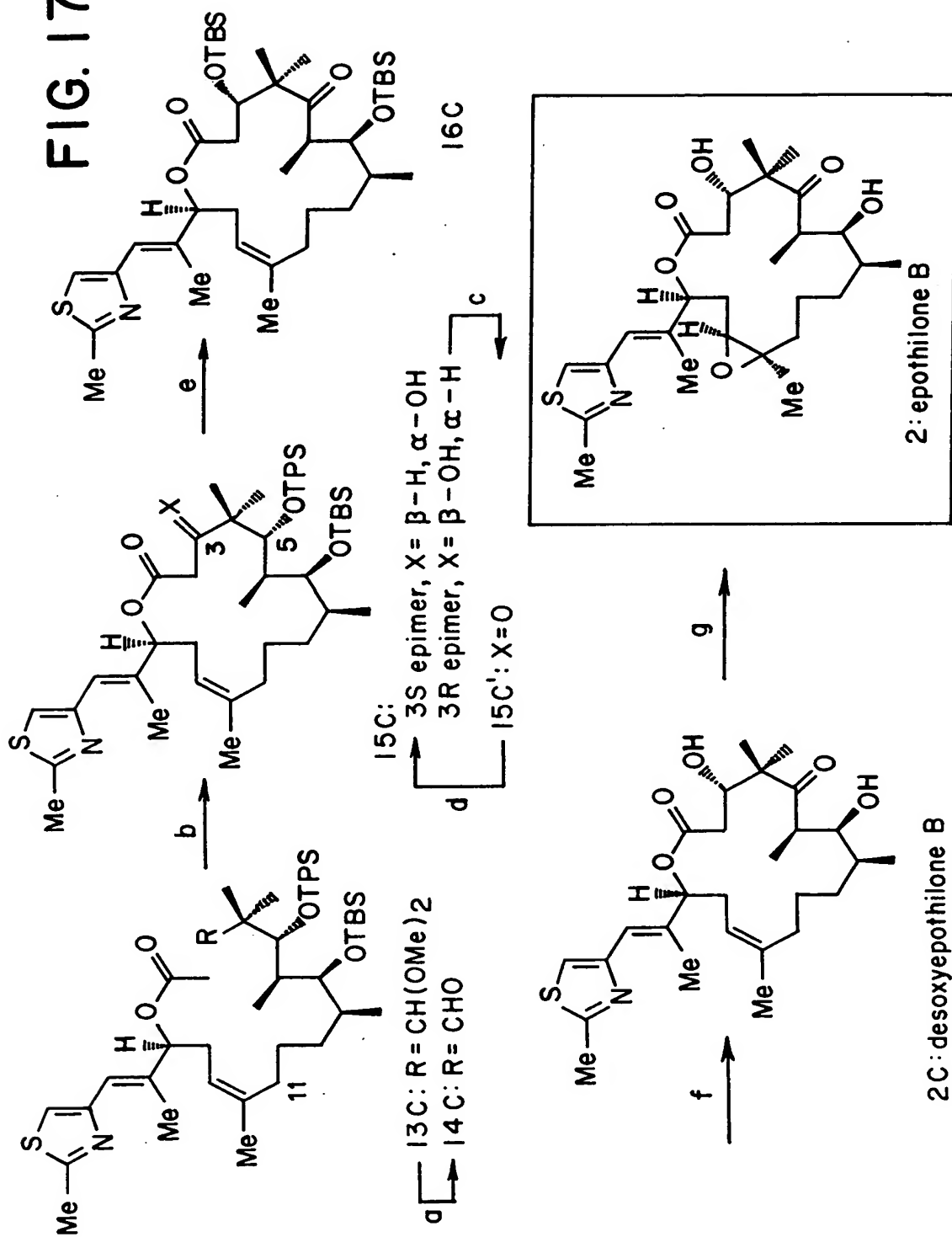


FIG. 17



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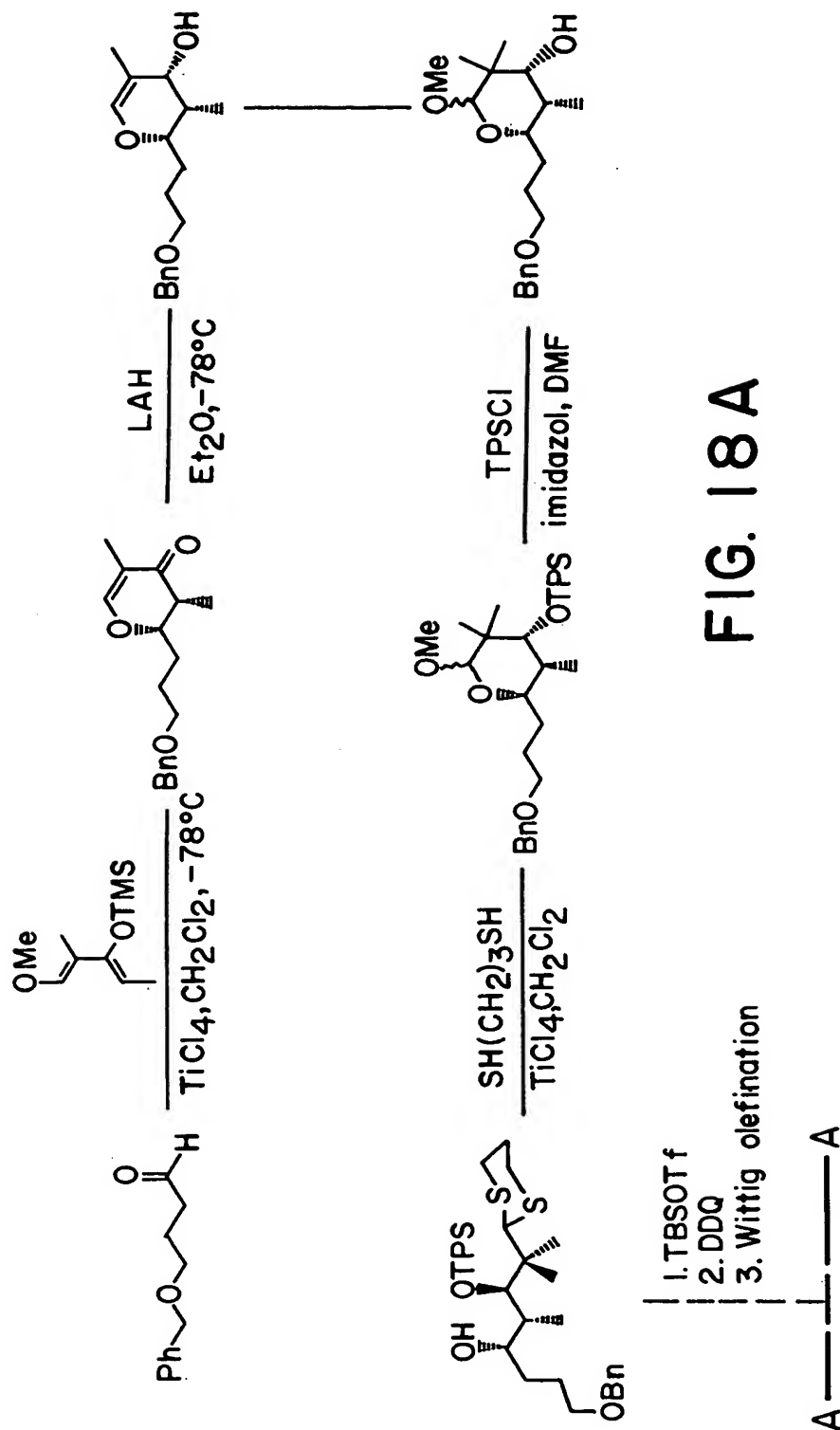


FIG. 18A

FIG. 18B

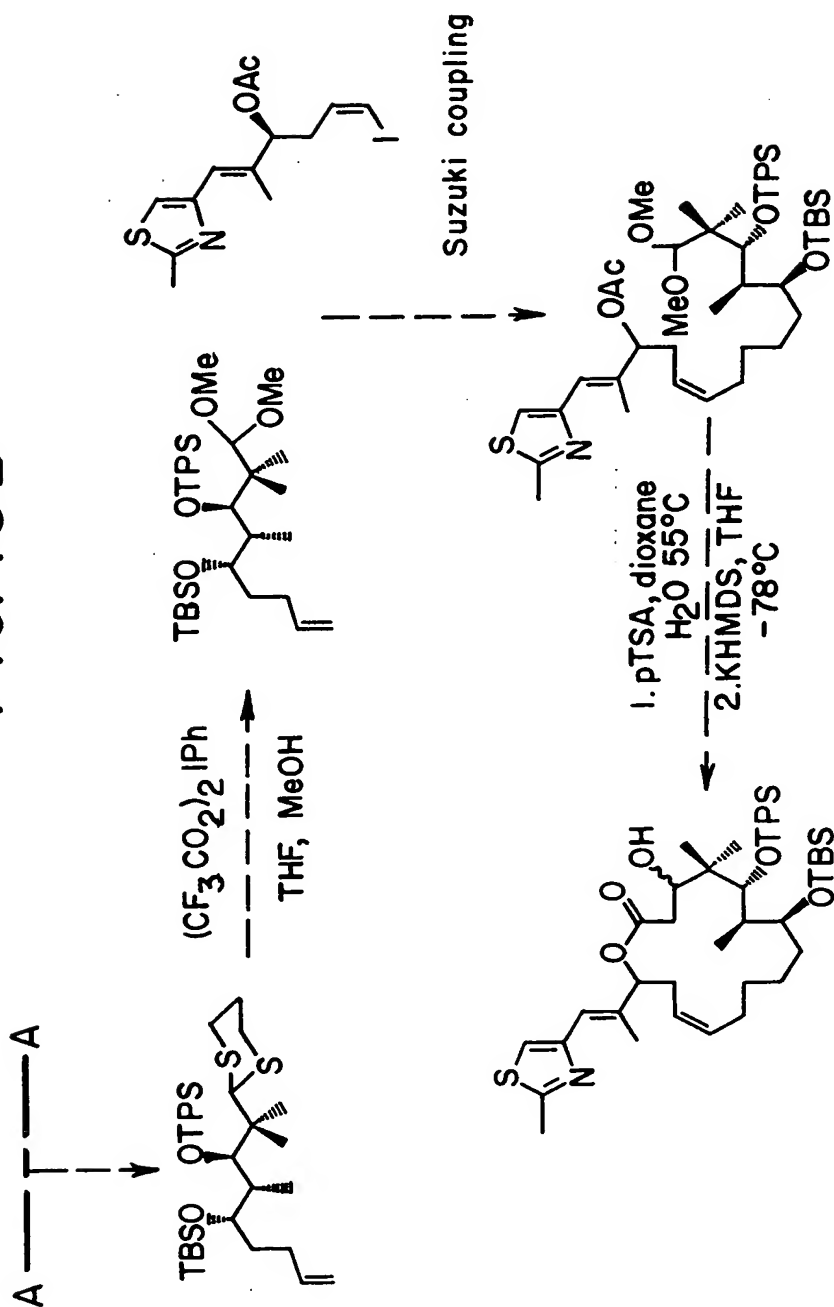


FIG. 19A

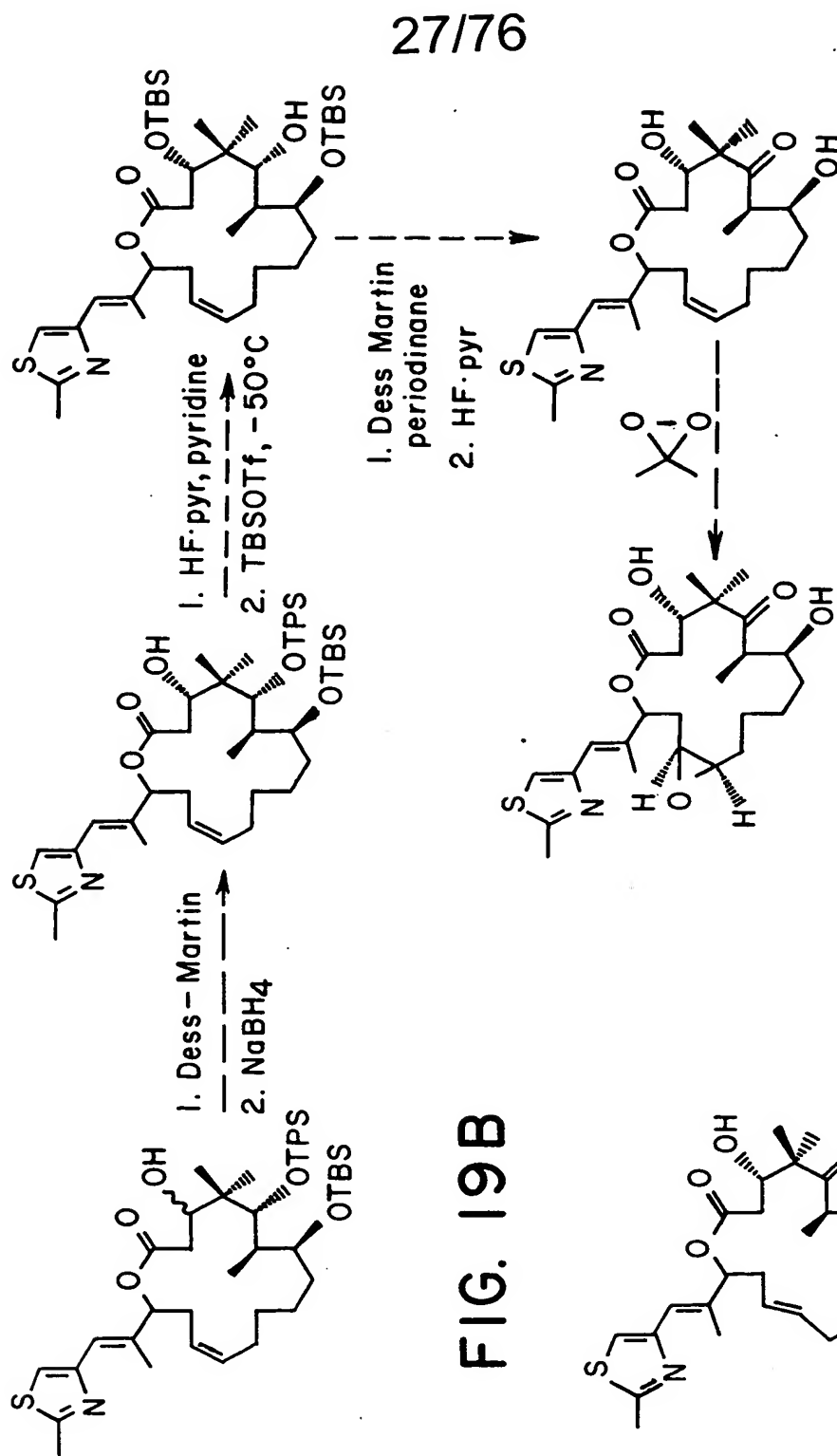
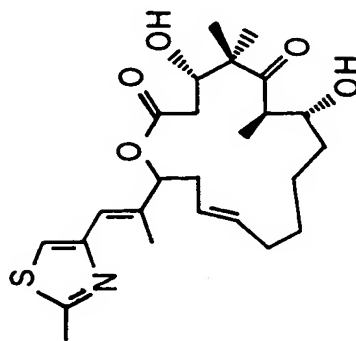


FIG. 19B



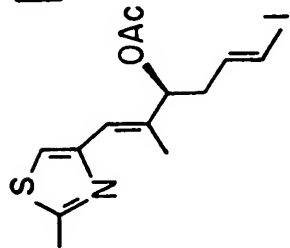


FIG. 19C

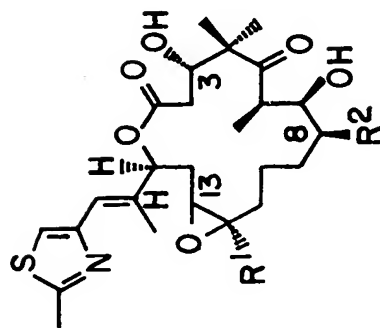


FIG. 20A

$R^1 = H, R^2 = \text{Me}$; epothilone A

$R^1 = R^2 = \text{Me}$; epothilone B

$R^1 = R^2 = H$; Cg - desmethyl - epothilone A (3D)

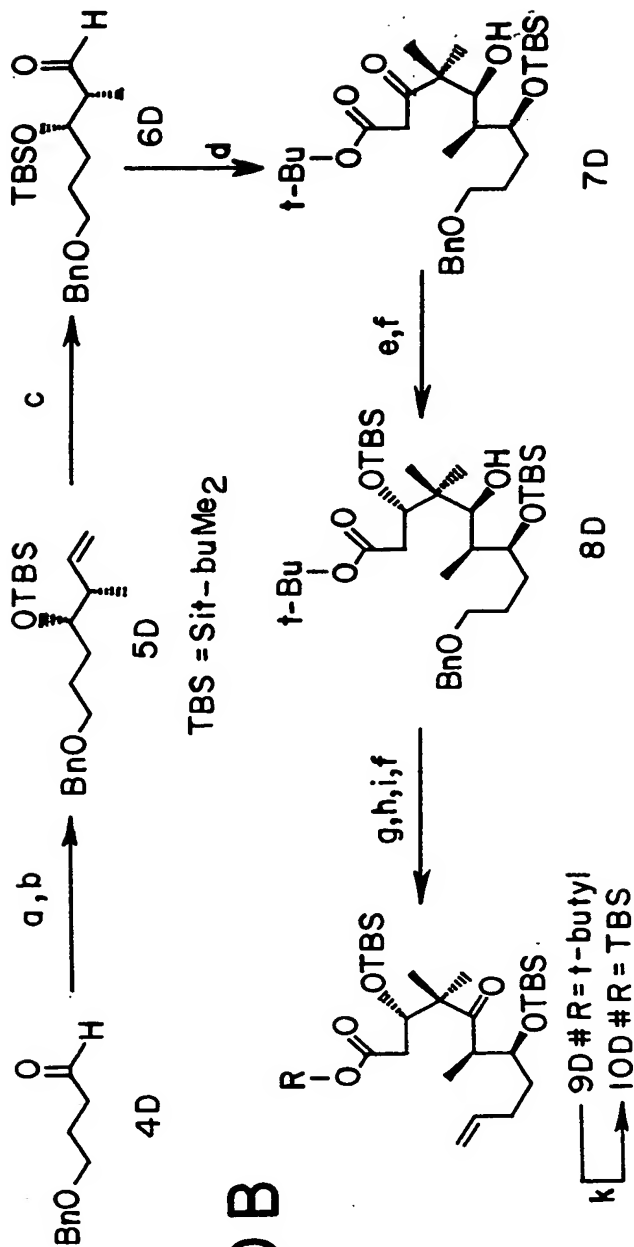


FIG. 20B

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FIG. 21

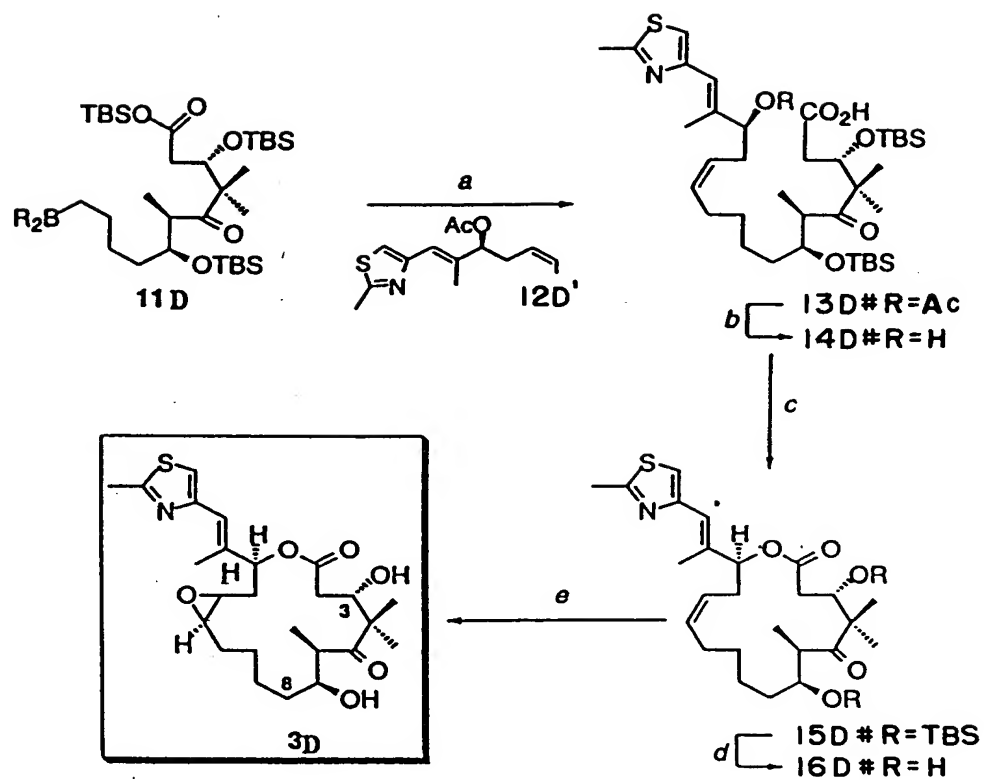


FIG. 22A

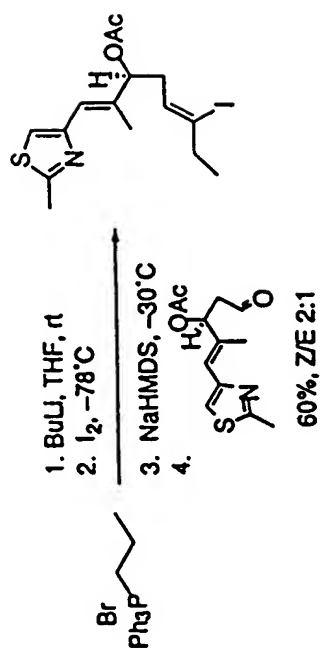


FIG. 22B

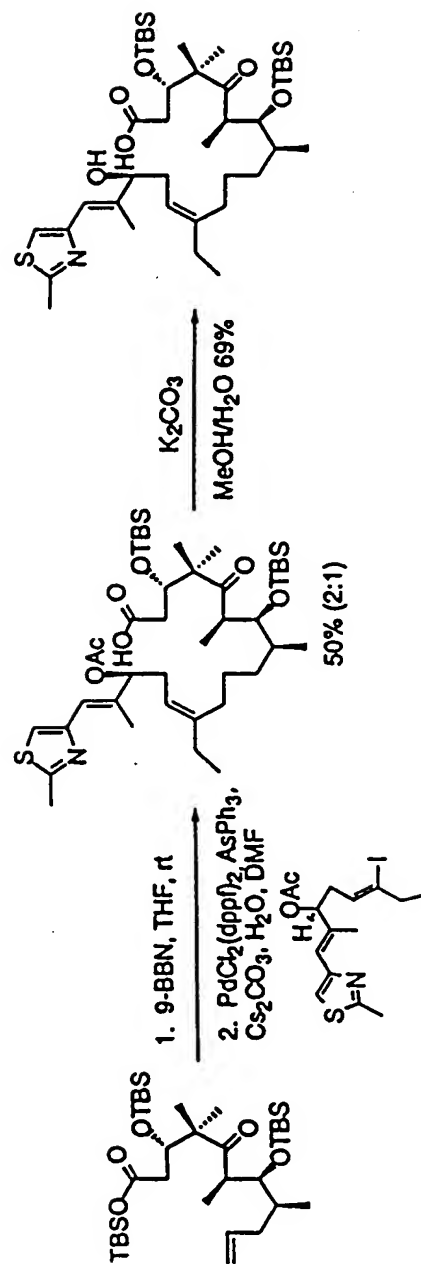


FIG. 22C

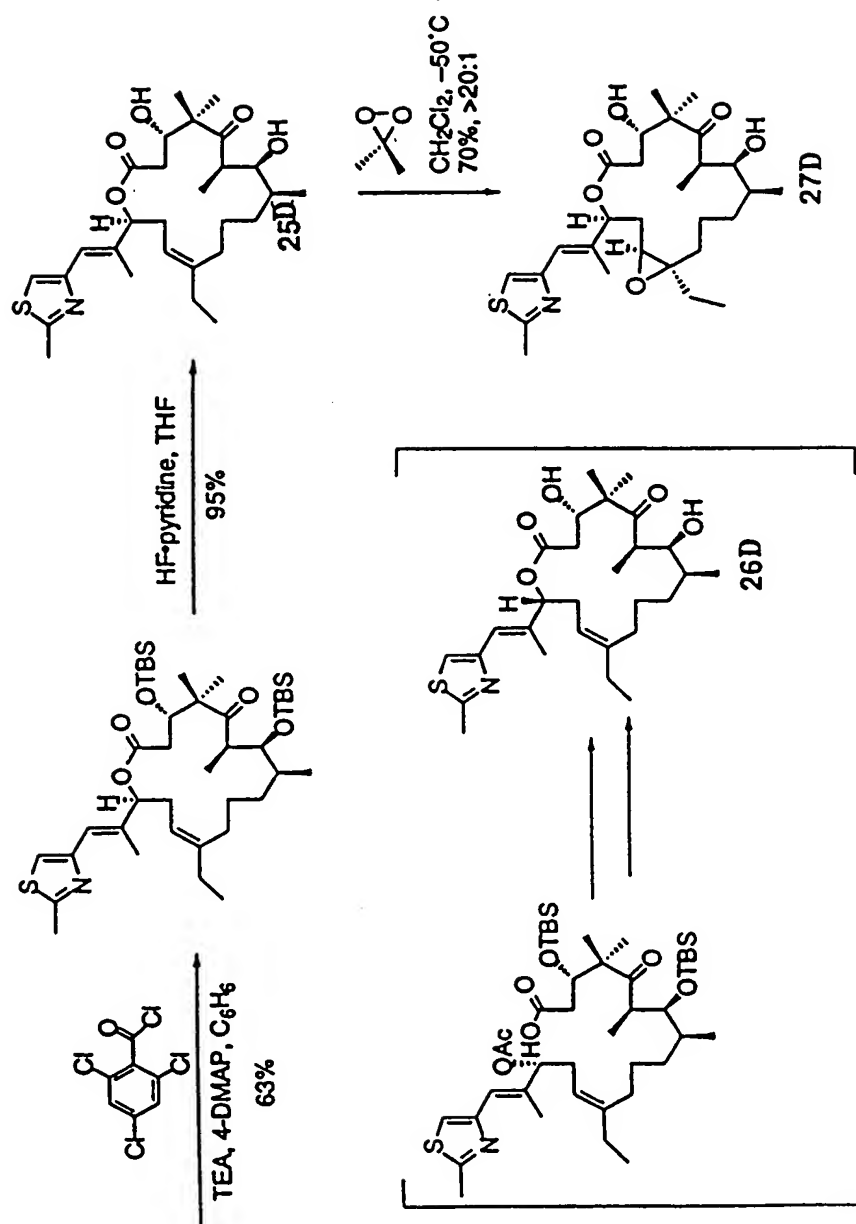


FIG. 23A

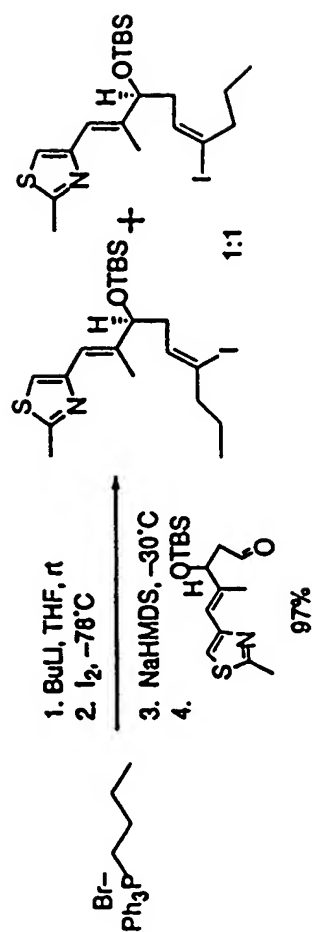


FIG. 23B

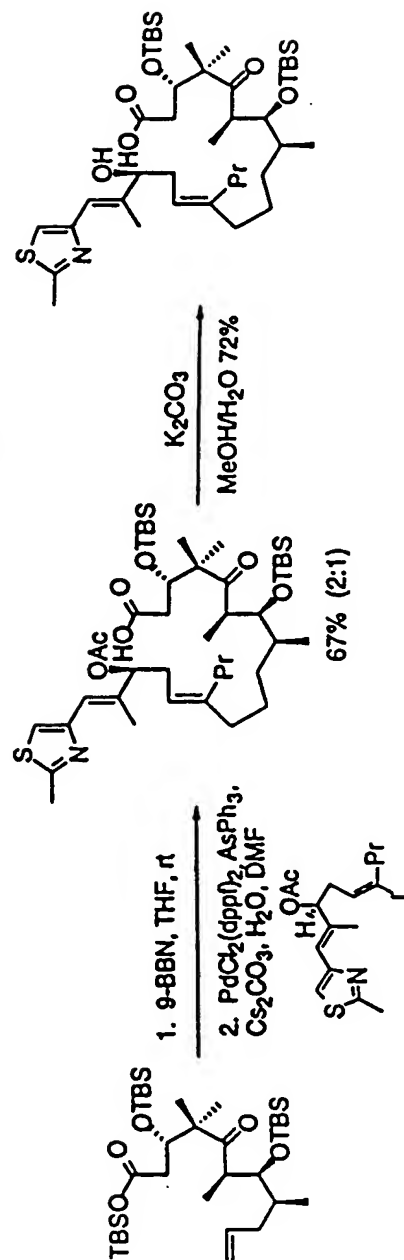


FIG. 23C

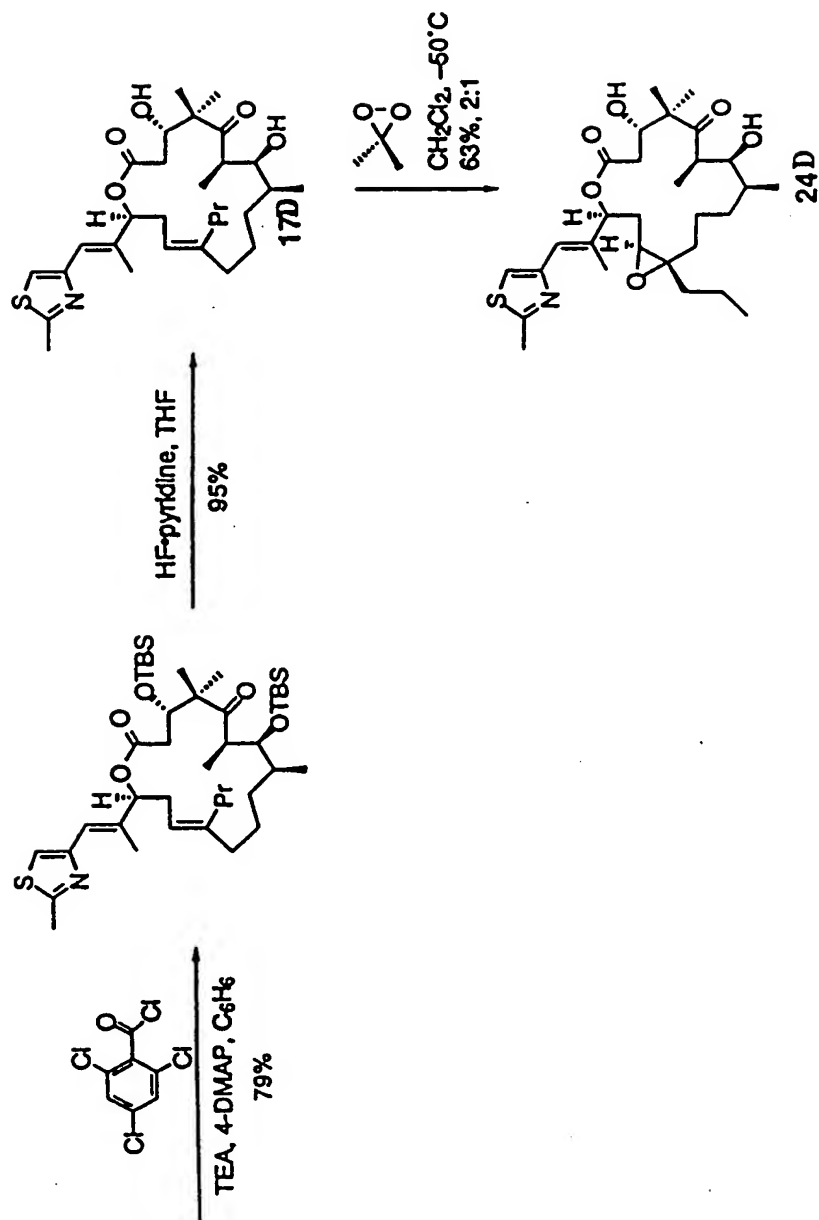


FIG. 24A

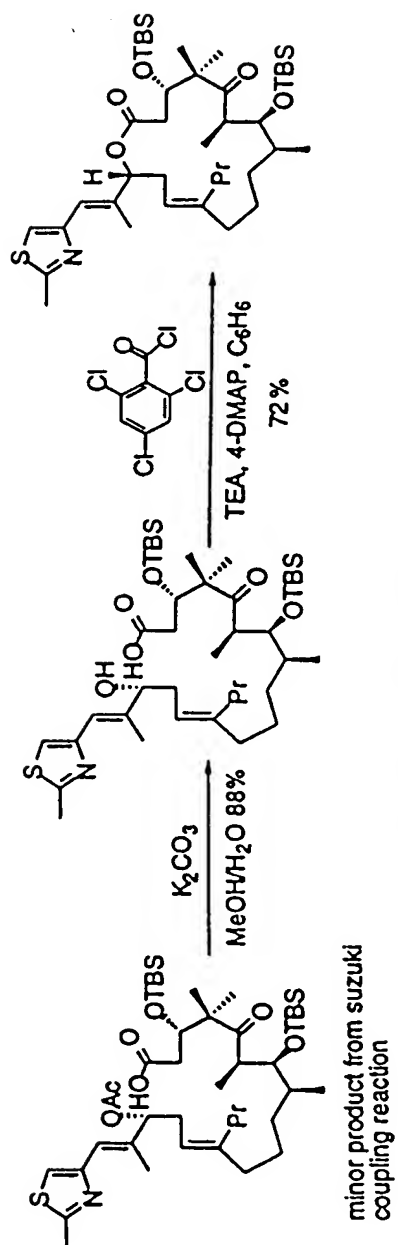


FIG. 24B

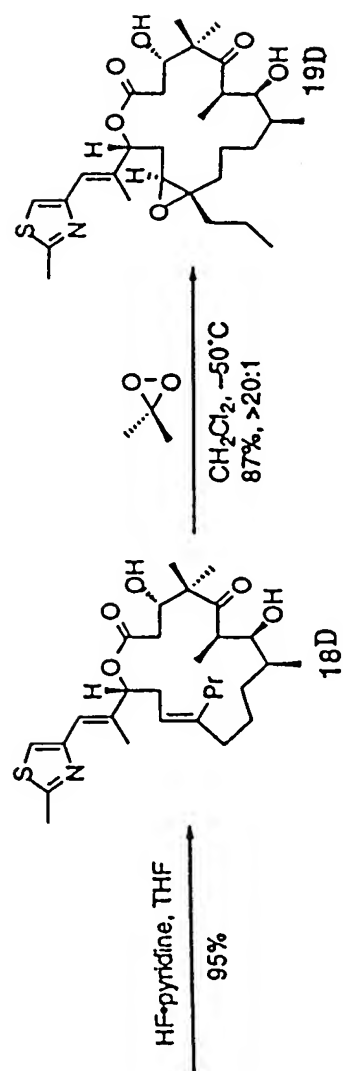


FIG. 25A

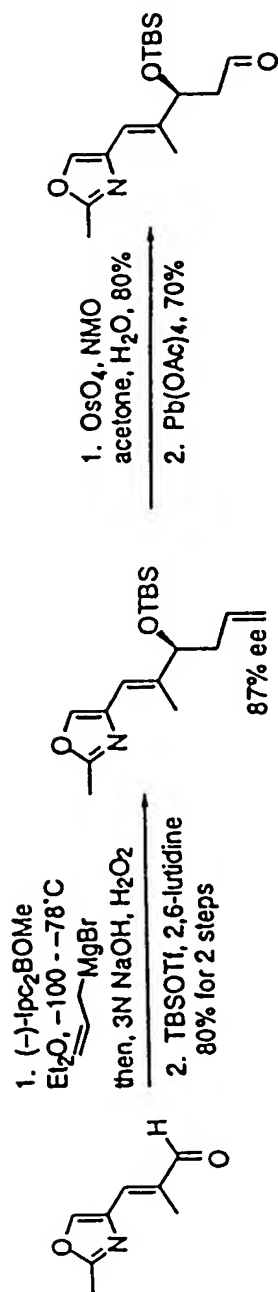


FIG. 25B

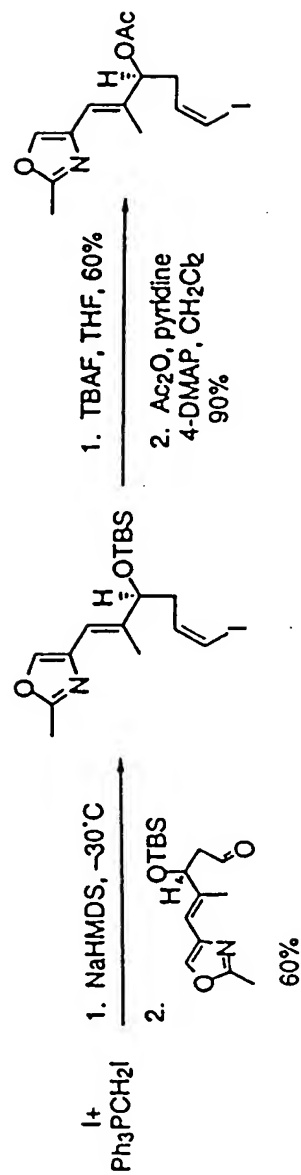


FIG. 25C

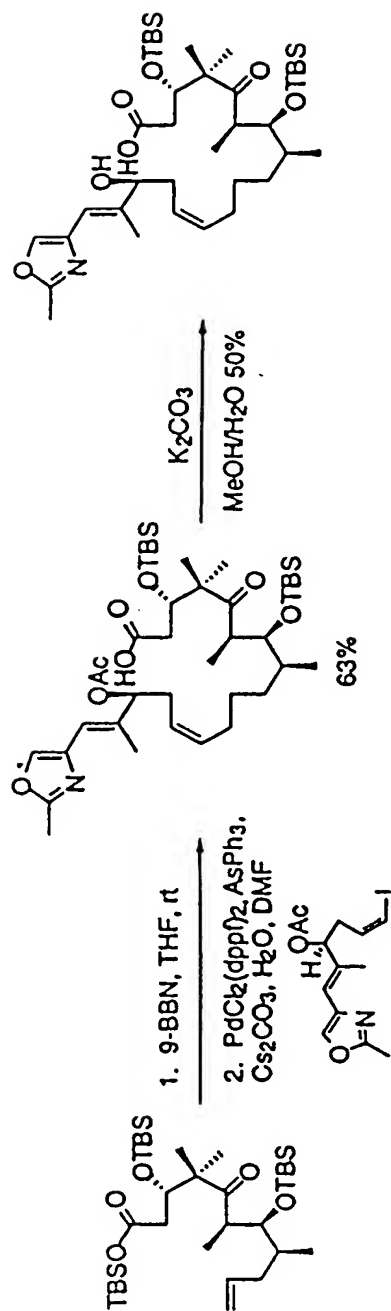


FIG. 25D

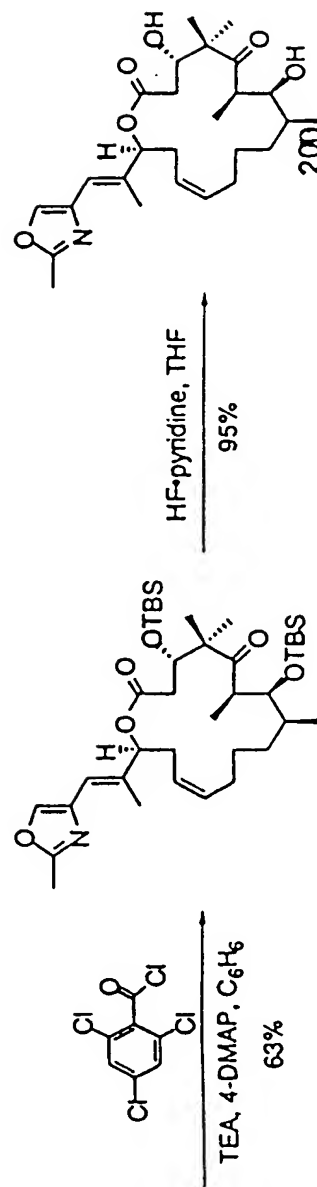


FIG. 26A

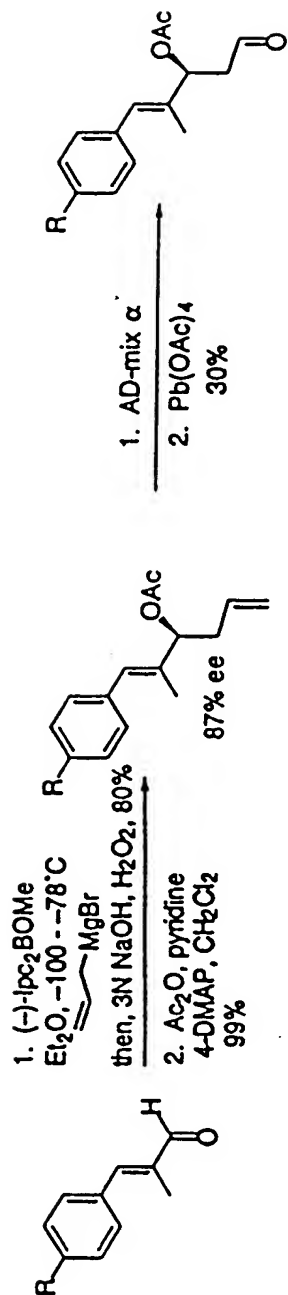
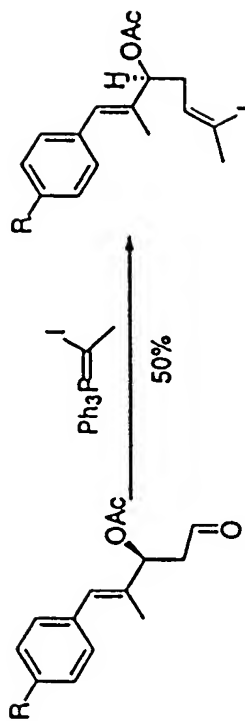


FIG. 26B



R = H, F, CF_3
 R=H is the only compound
 completed, F and CF_3 are nearly
 completed

FIG. 26C

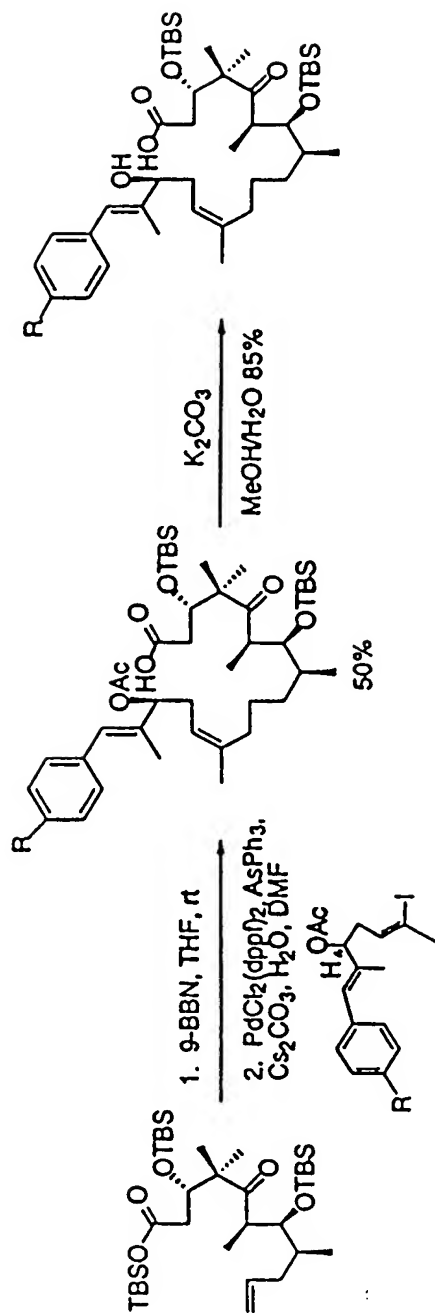


FIG. 26D

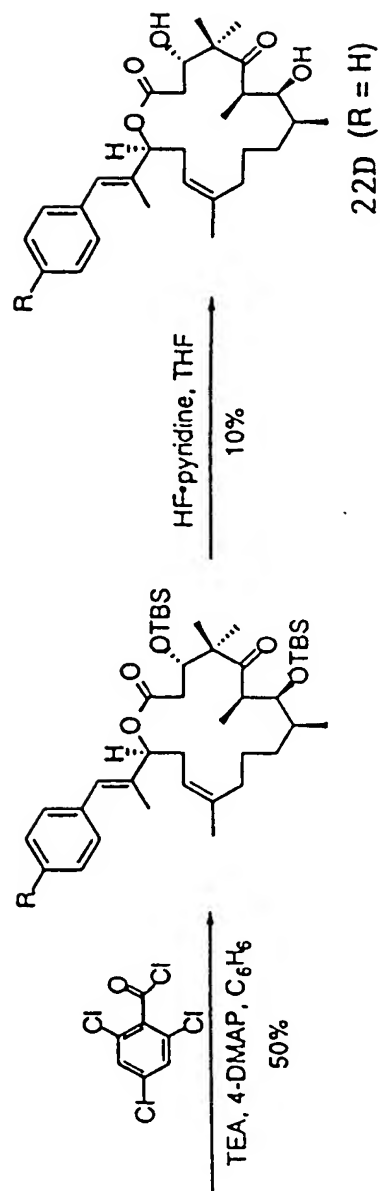


FIG. 27A

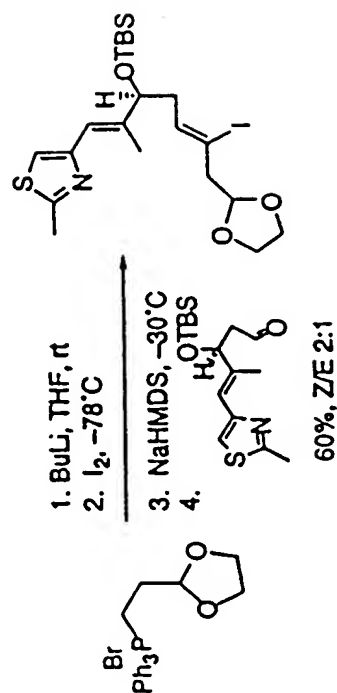


FIG. 27B

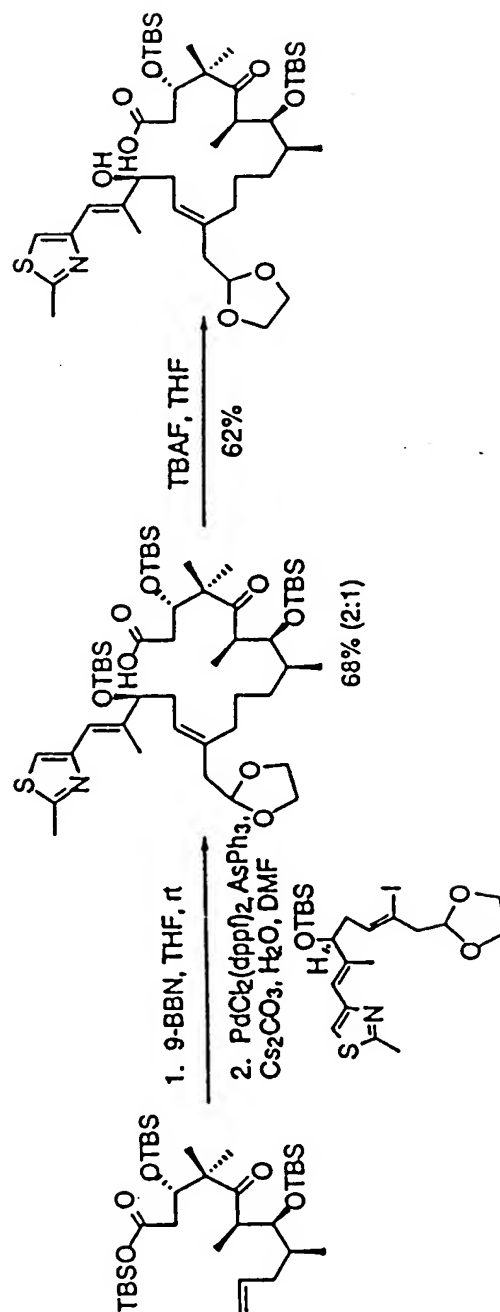
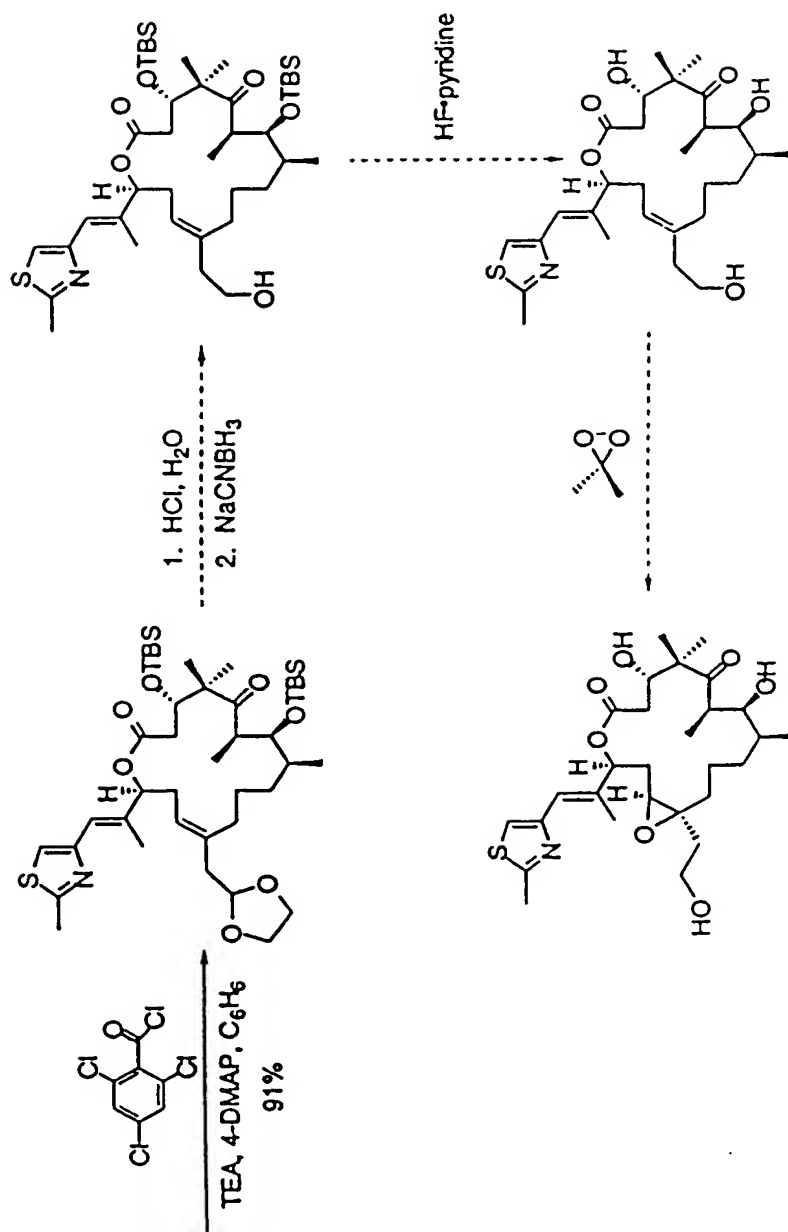


FIG. 27C



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FIG. 28A

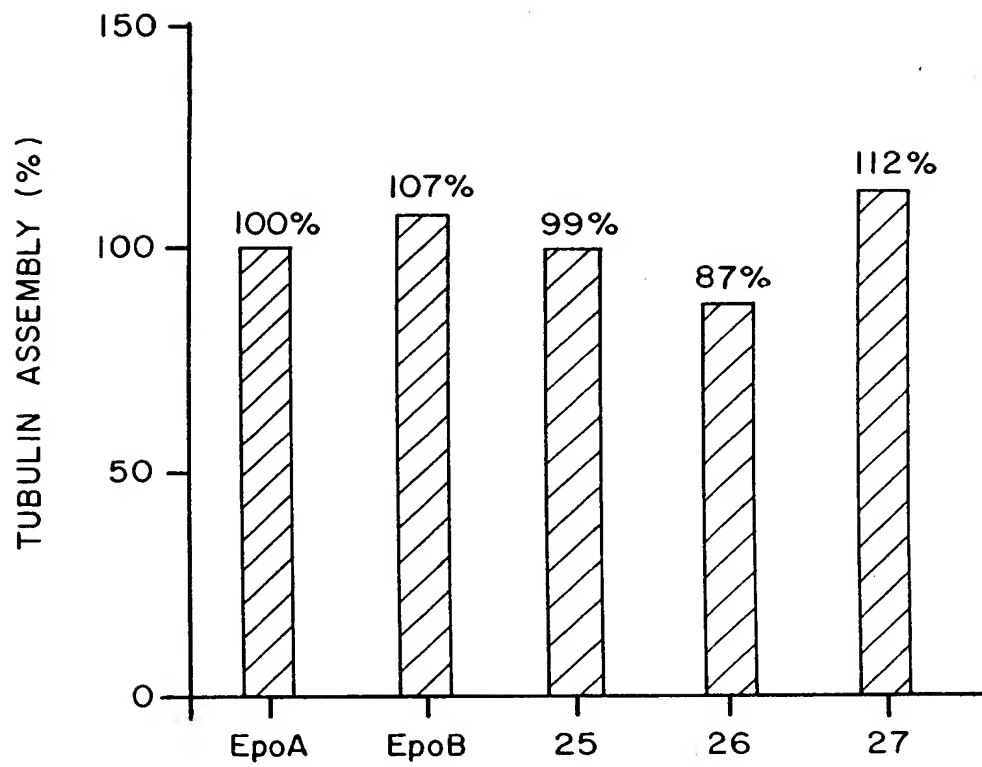
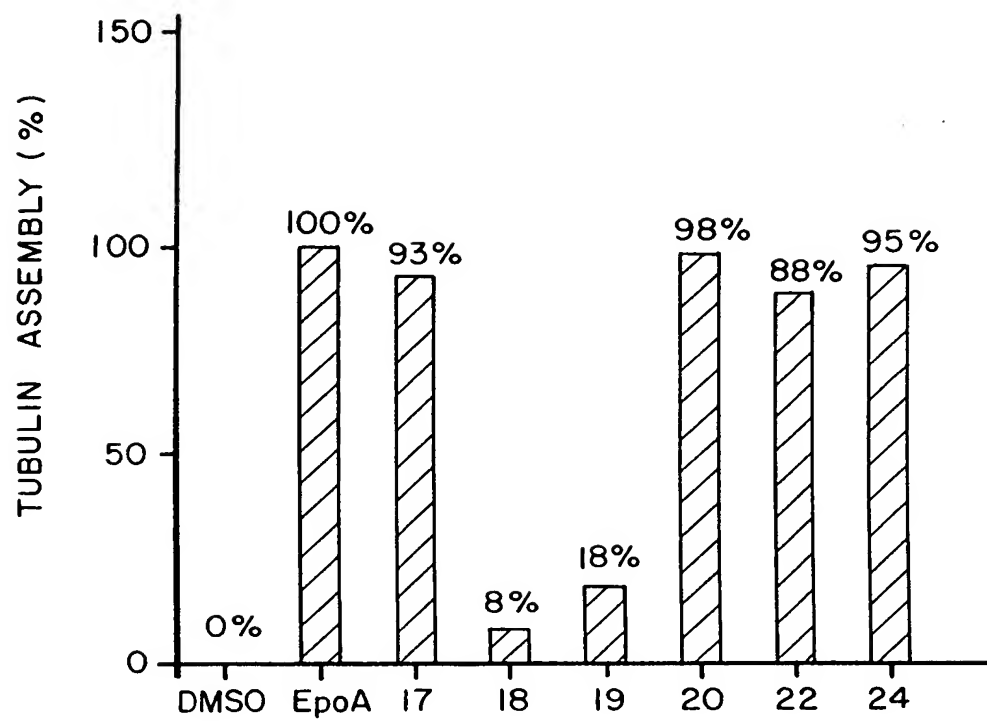


FIG. 28B



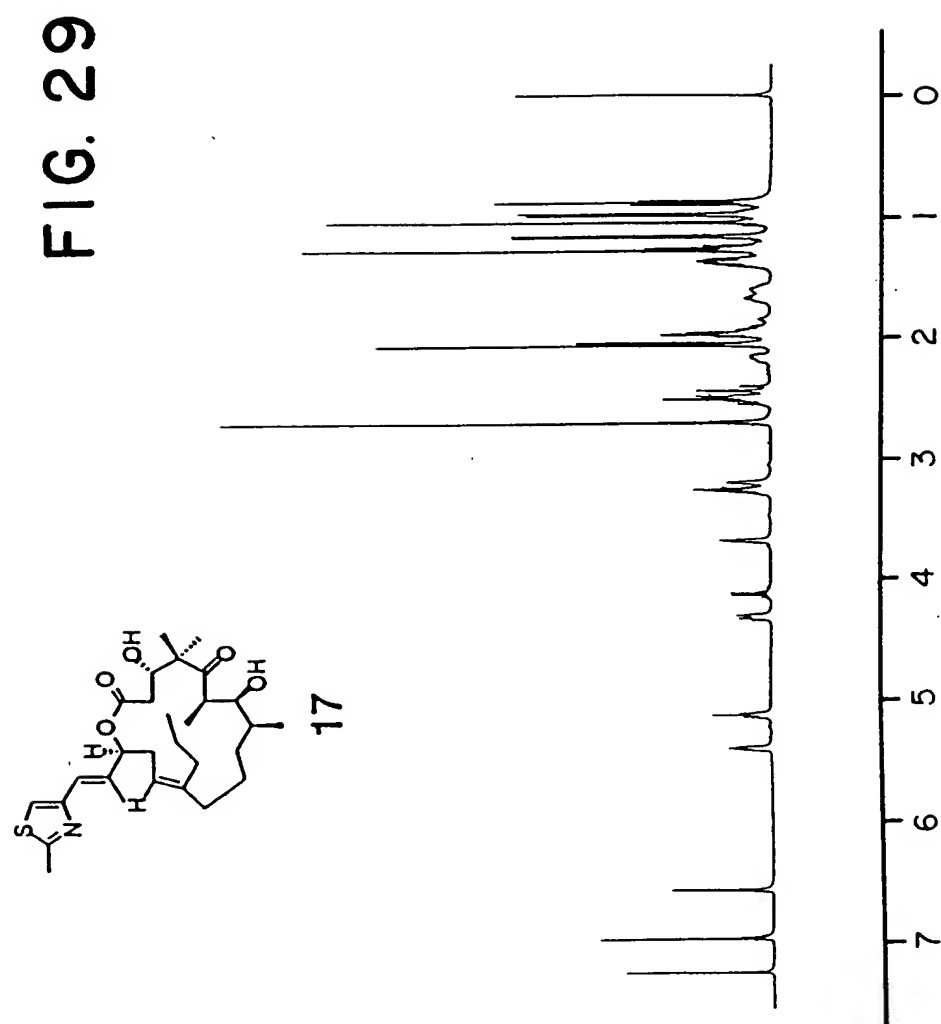
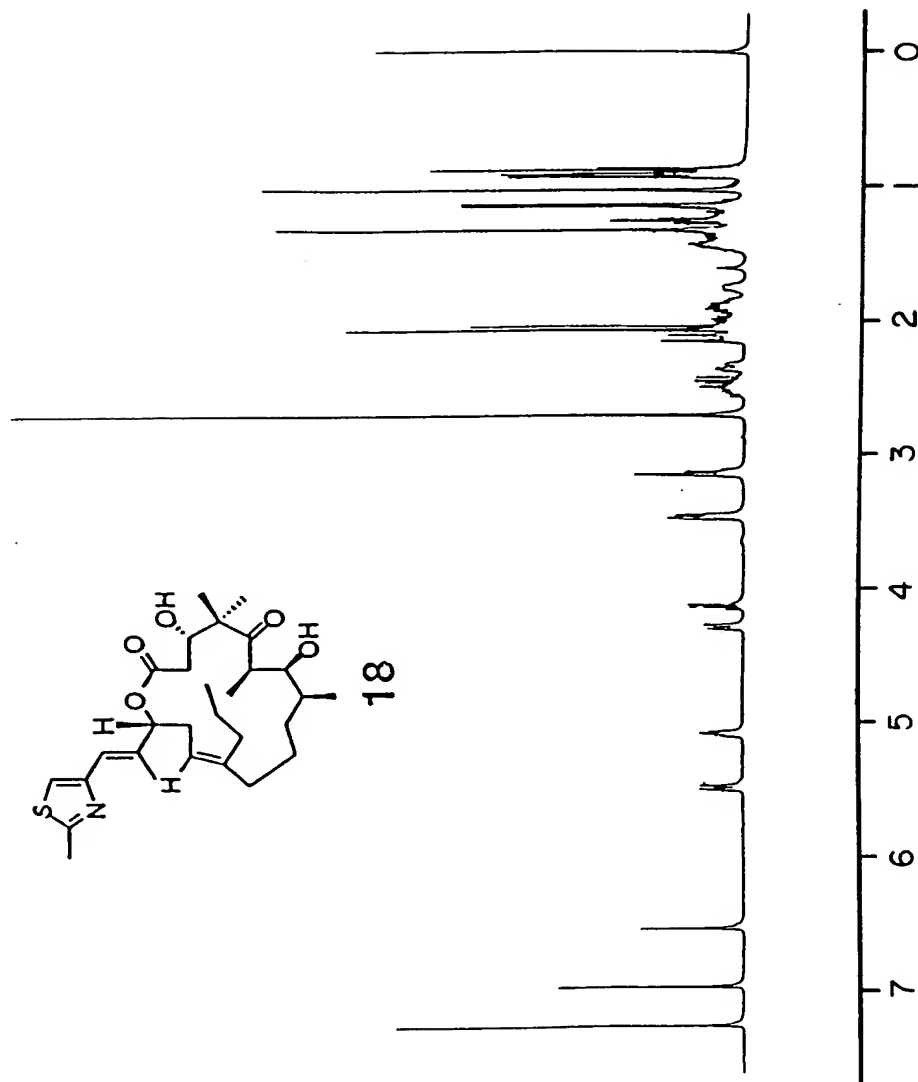


FIG. 30



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FIG. 31

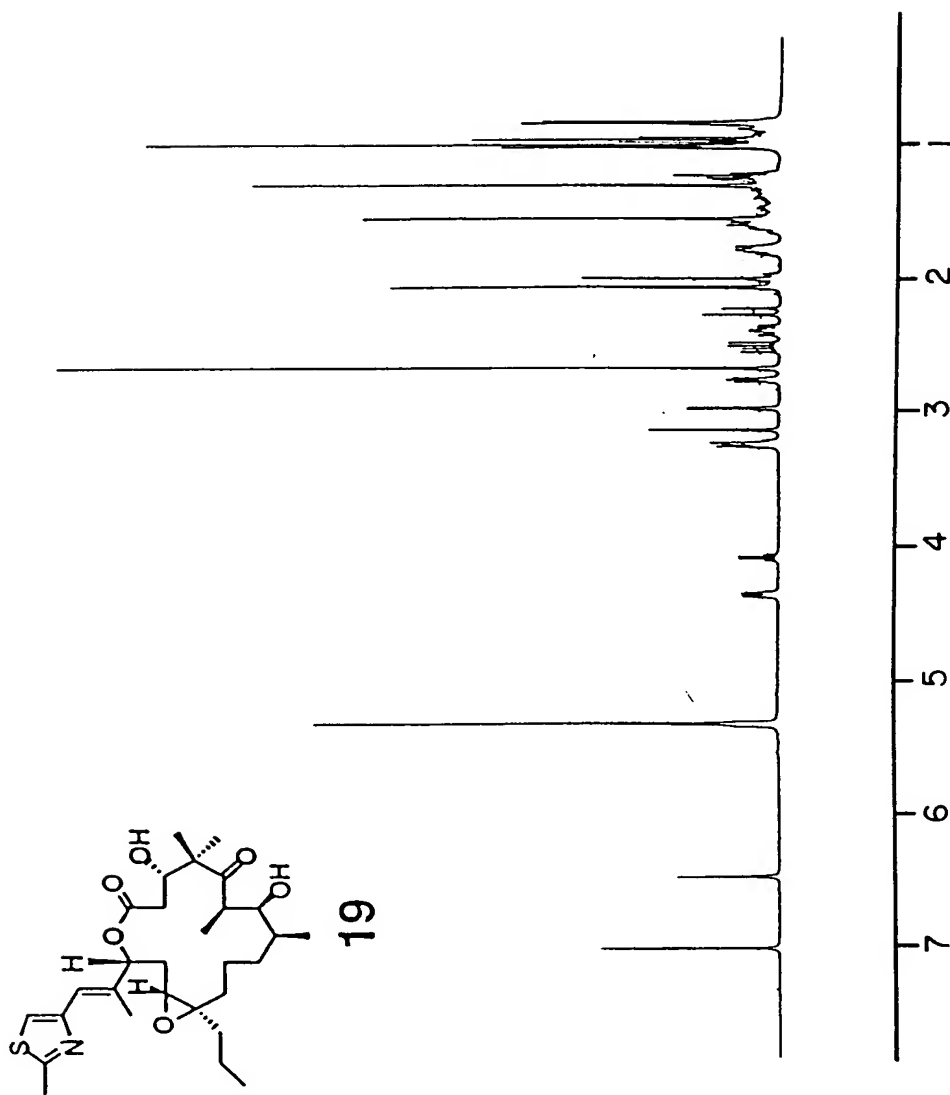


FIG. 32

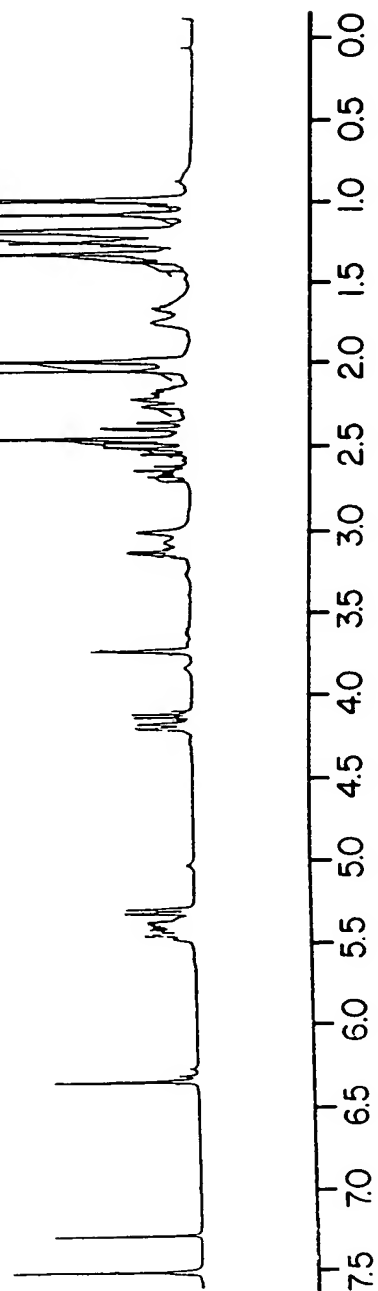
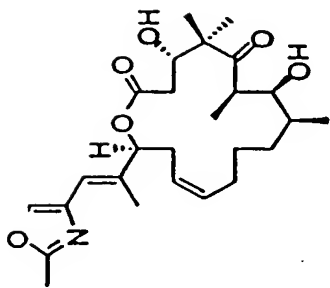
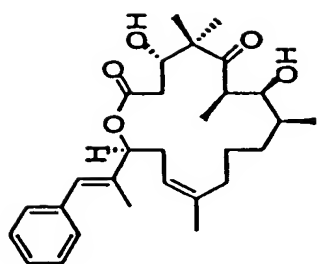
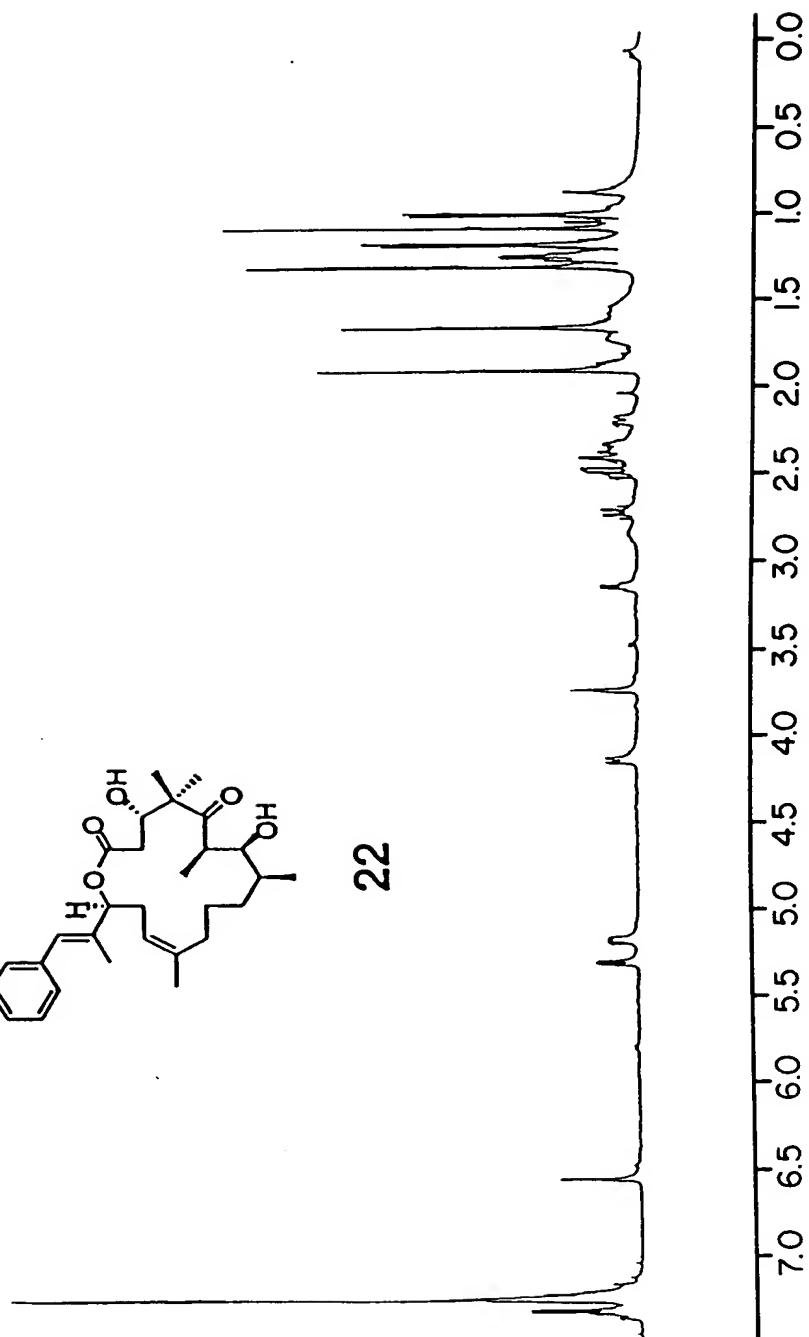


FIG. 33



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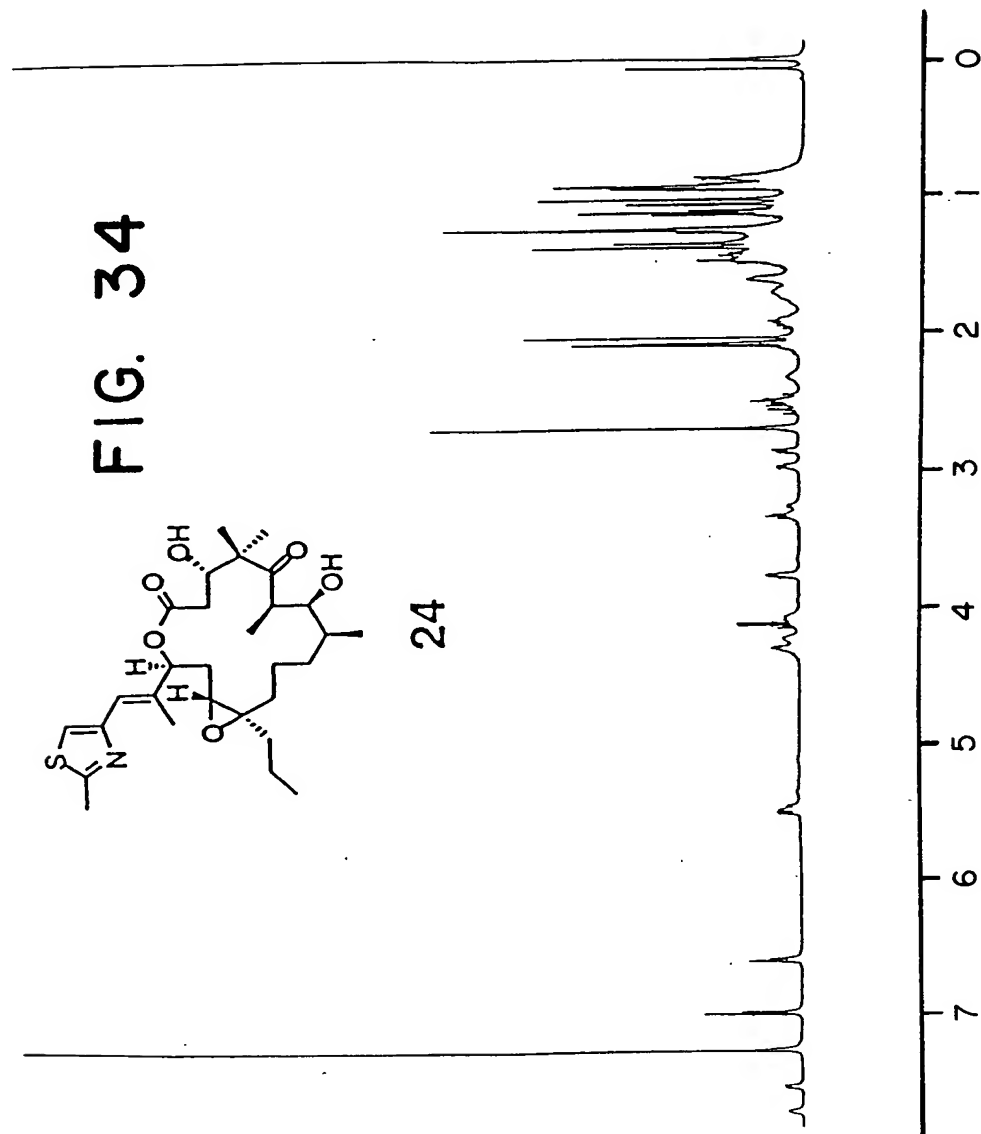
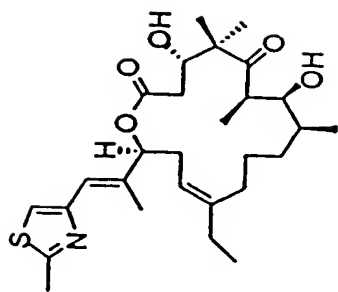


FIG. 35



25

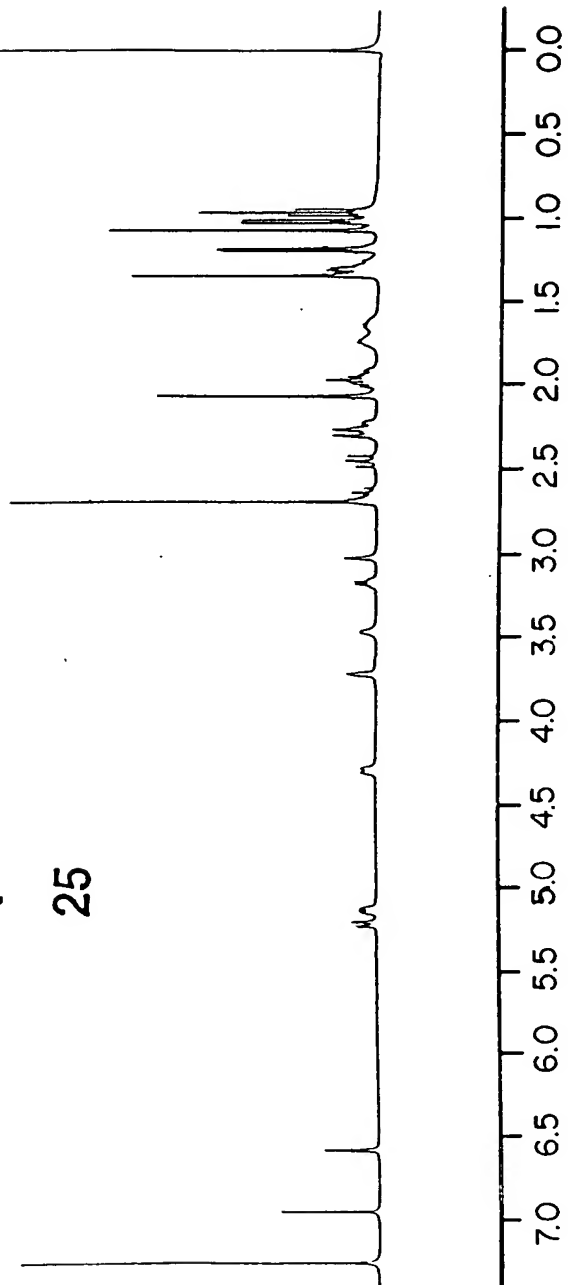
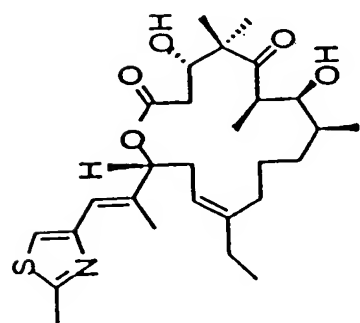


FIG. 36



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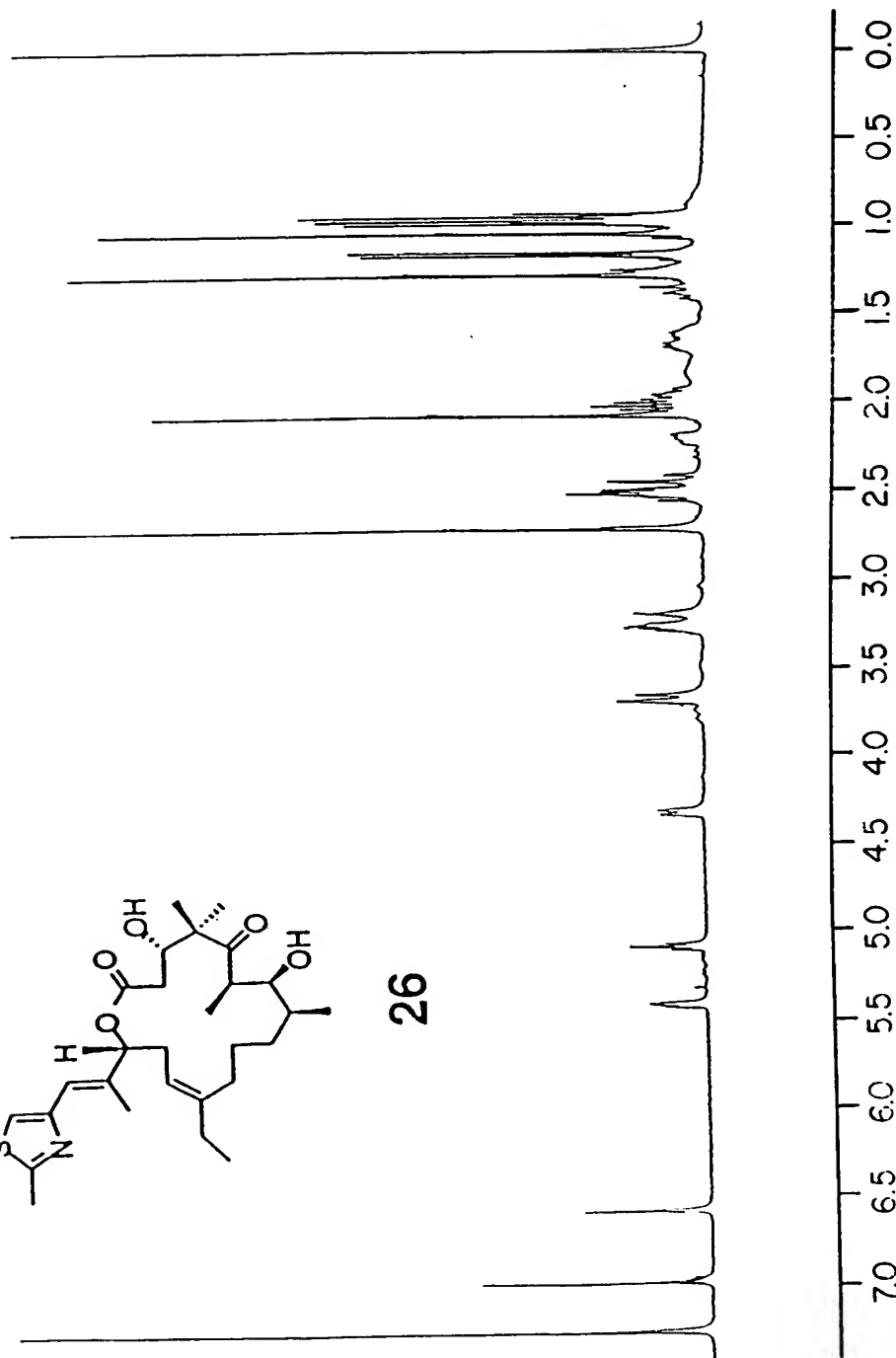


FIG. 37

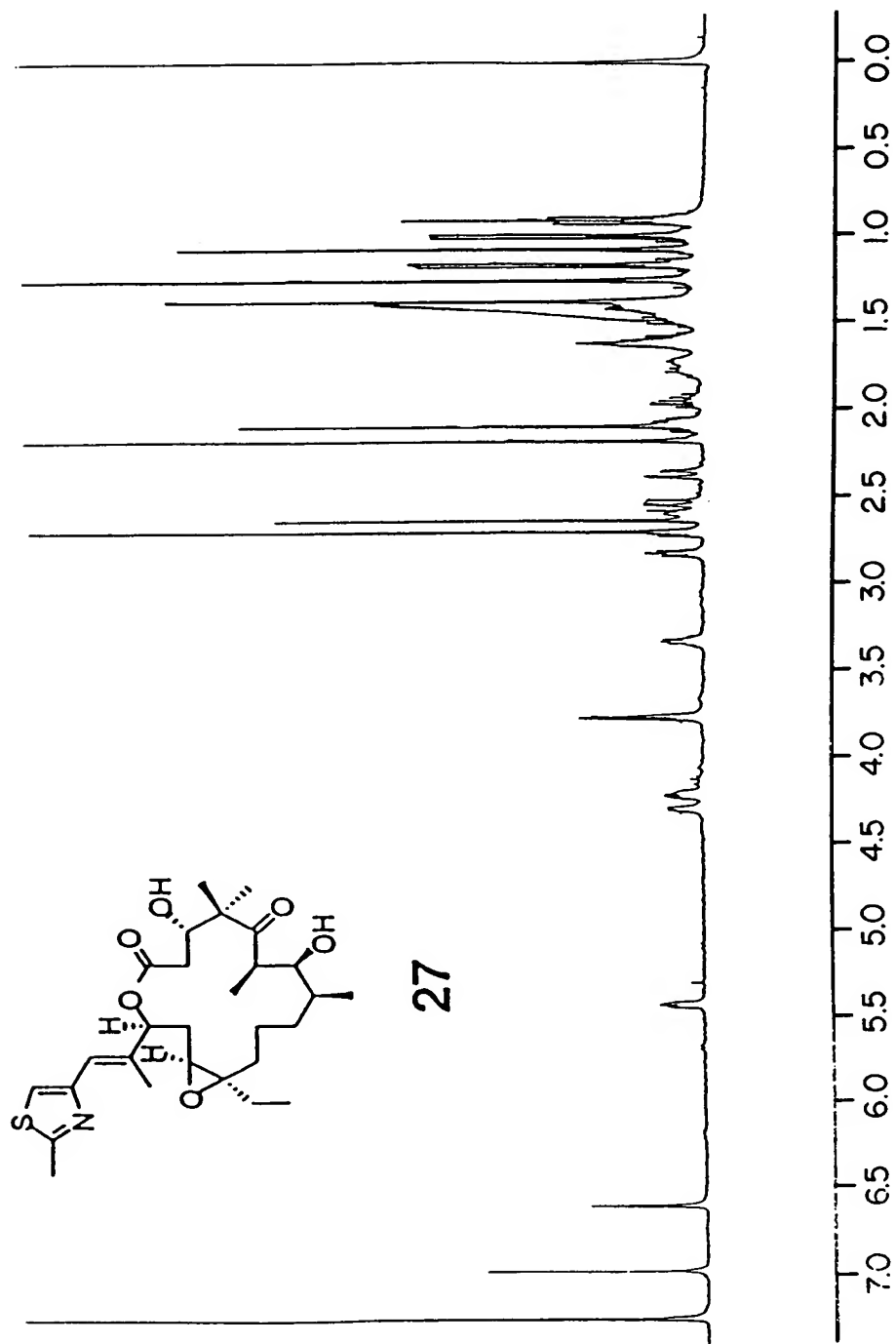
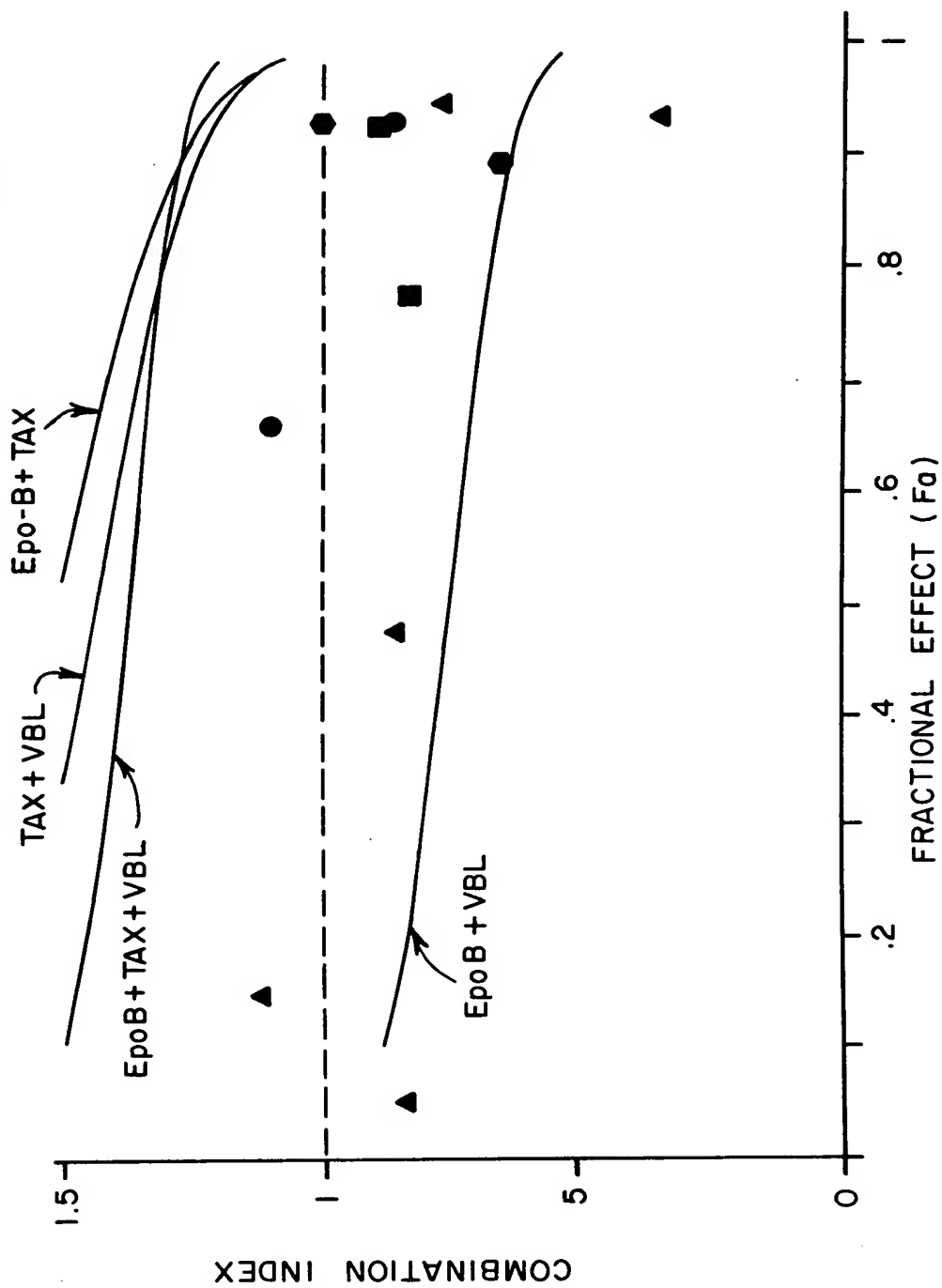
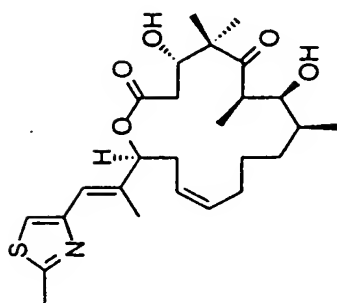


FIG. 38



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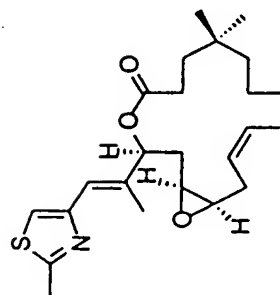
FIG. 39A



desoxyepothilone A

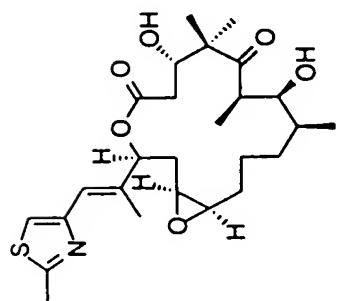
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(0.022)
[0.012]



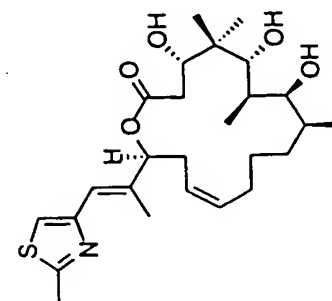
epothilone A

(0.0027)
[0.020]



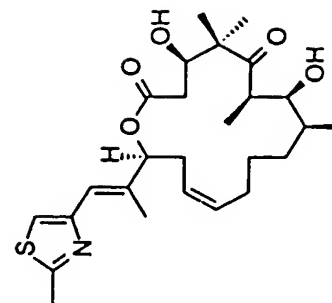
3

(271.1)
[22.4]



2

(14.23)
[6.28]

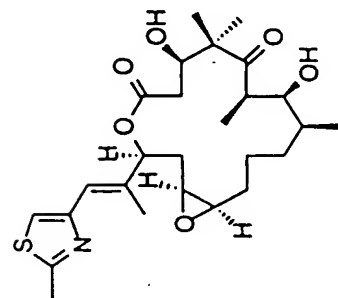


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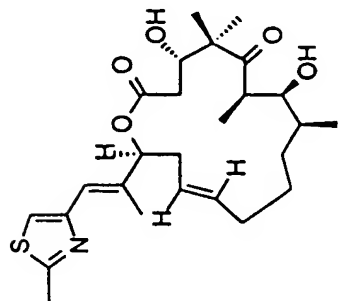
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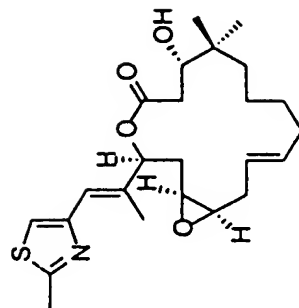
FIG. 39B



5
(>20)
[35.2]



6
(0.052)
[0.035]



7
(7.36)
[9.82]

FIG. 40A

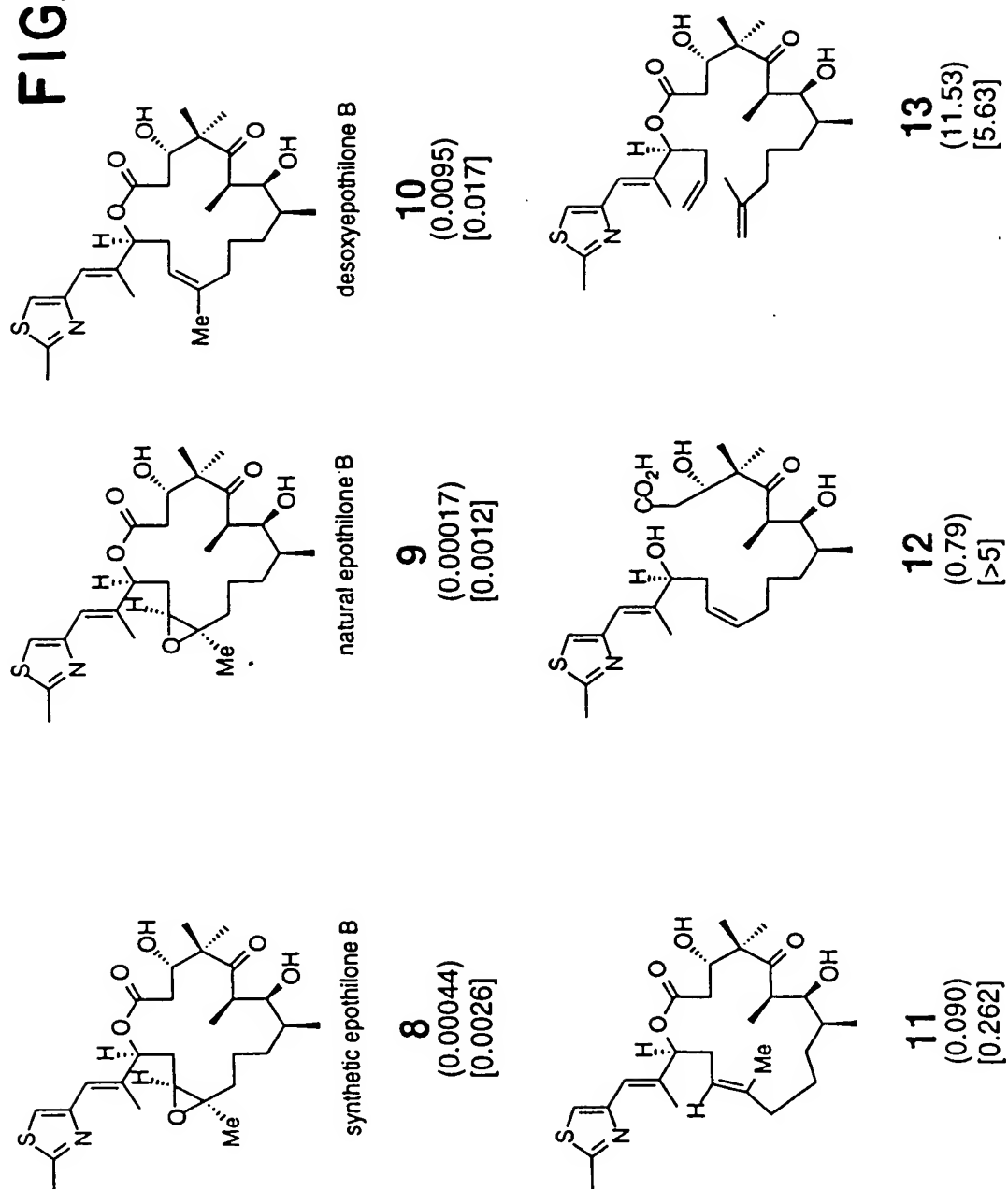


FIG. 40B

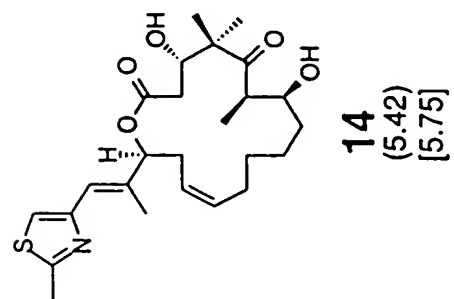
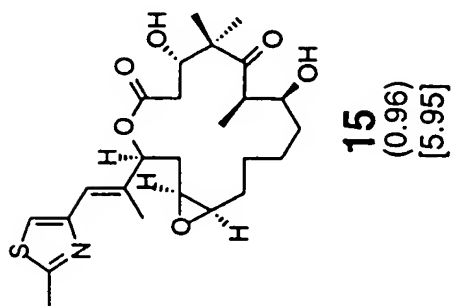
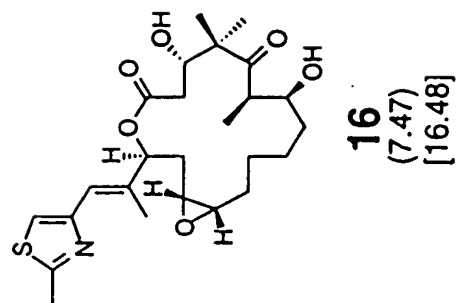
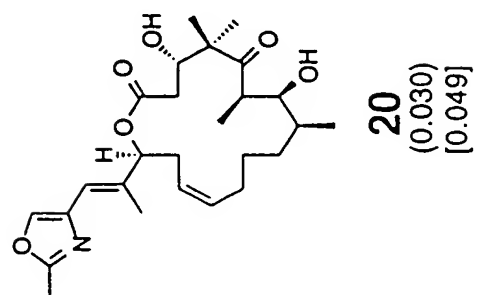
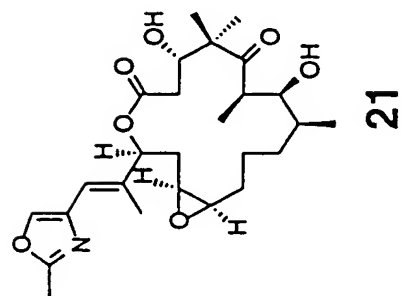
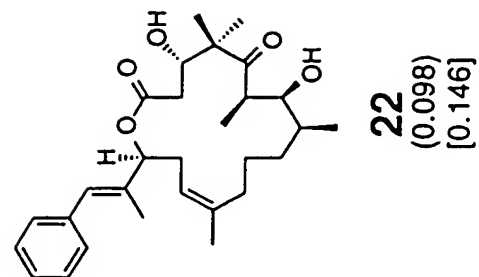
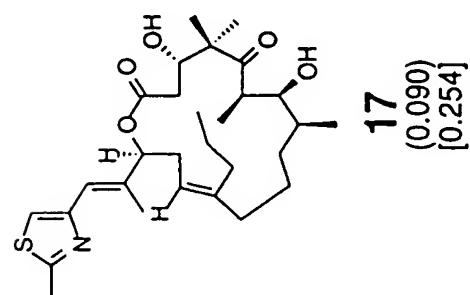
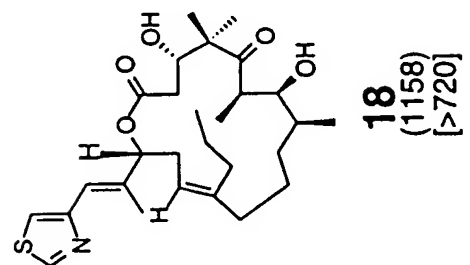
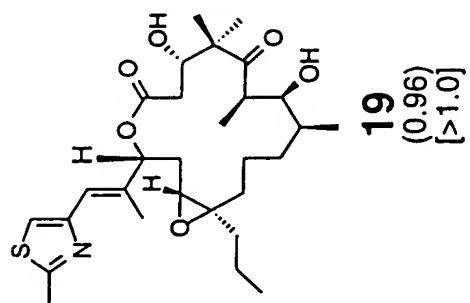


FIG. 41A



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FIG. 41B

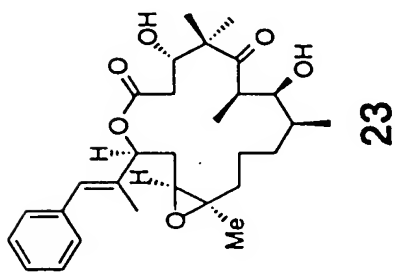
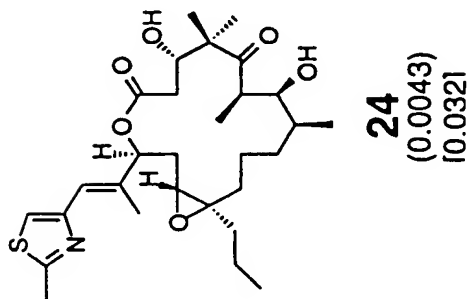
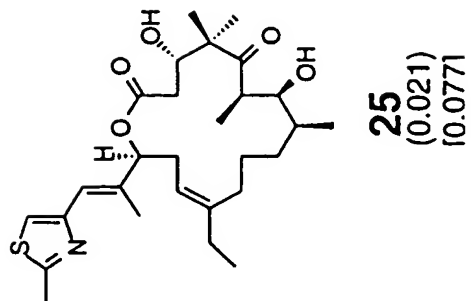


FIG. 42A

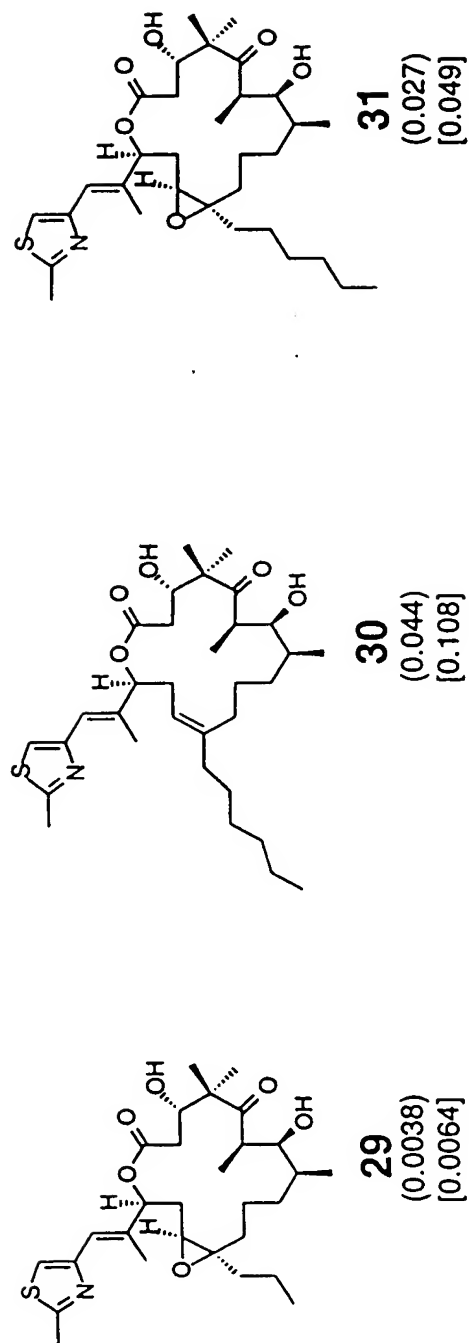
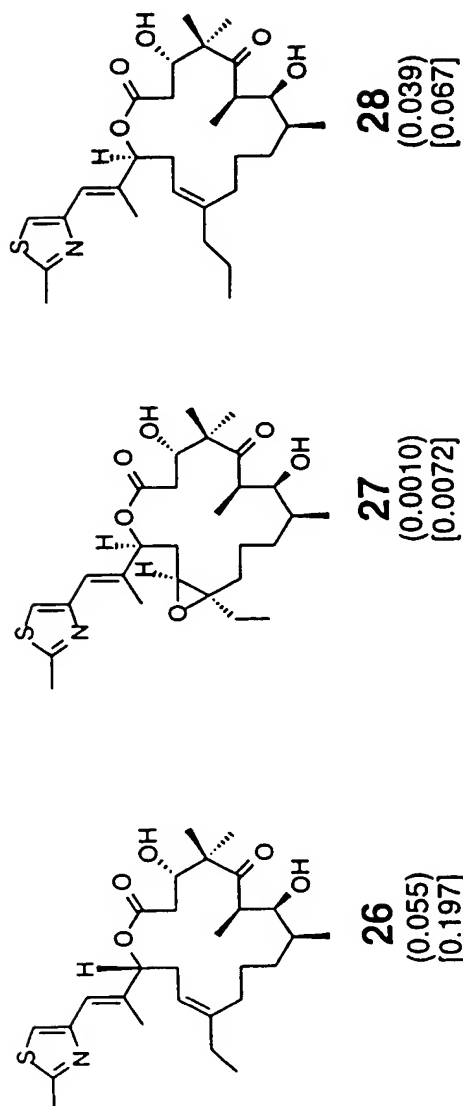


FIG. 42B

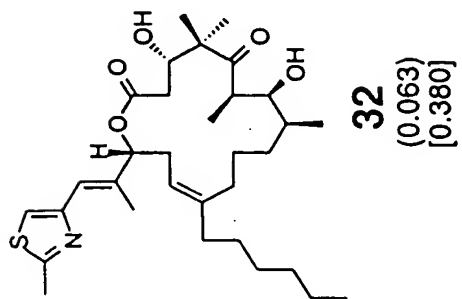
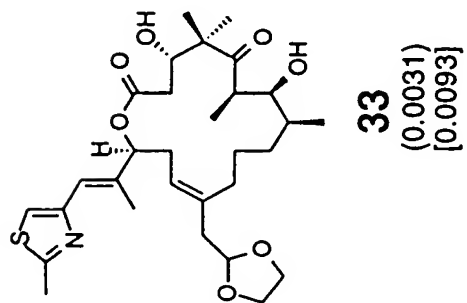
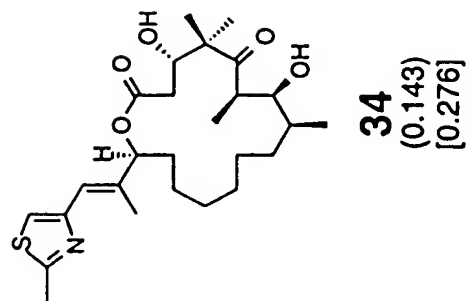


FIG. 42C

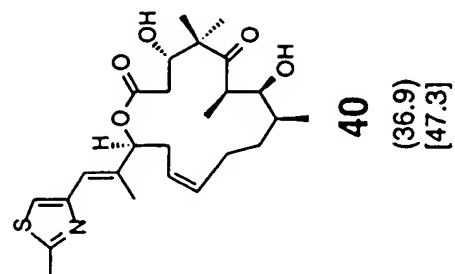
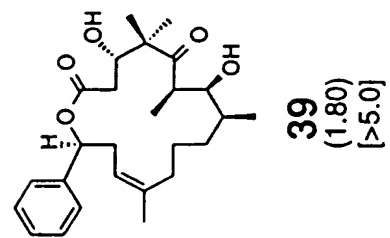
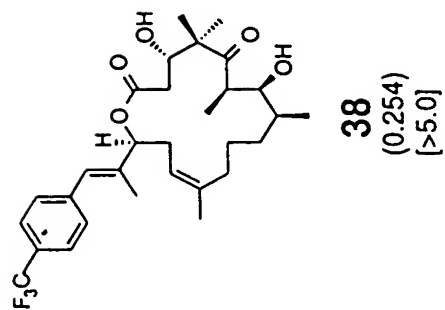
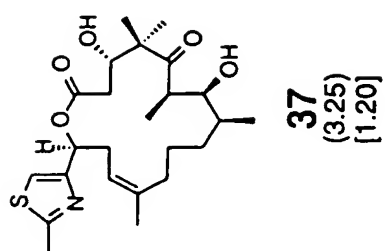
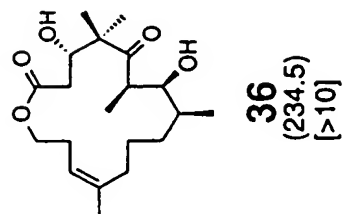
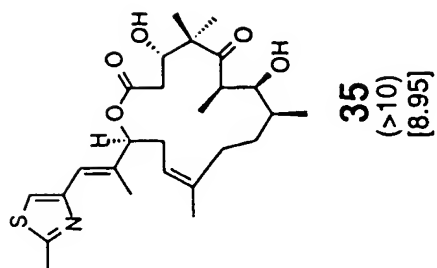
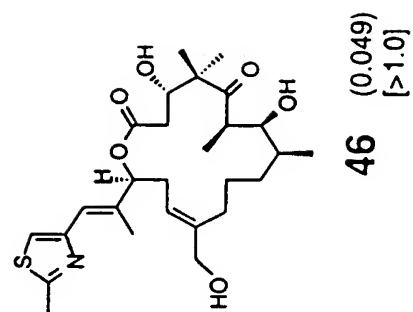
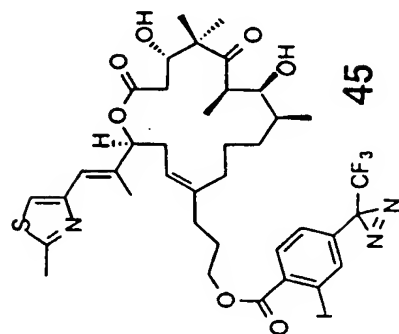
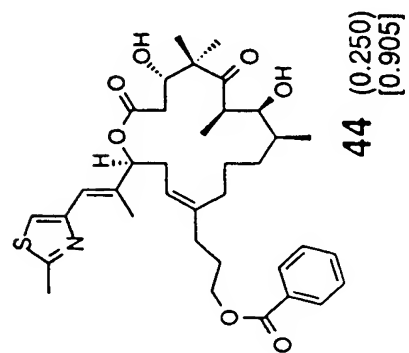
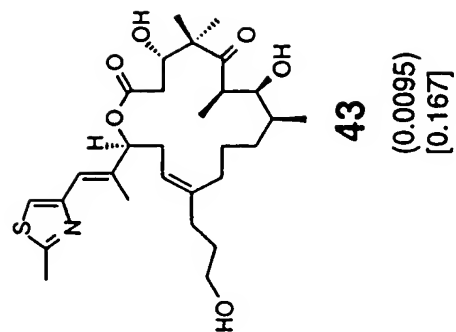
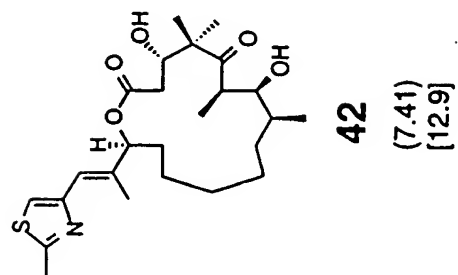
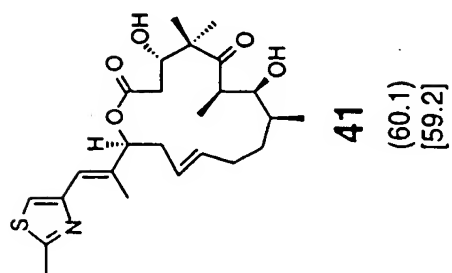
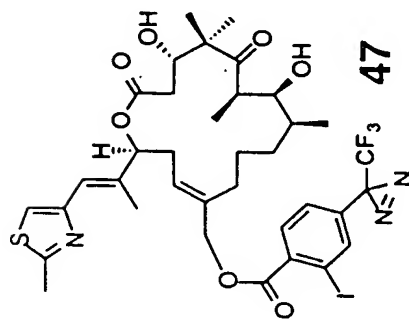
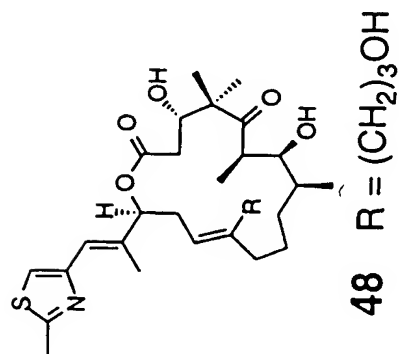
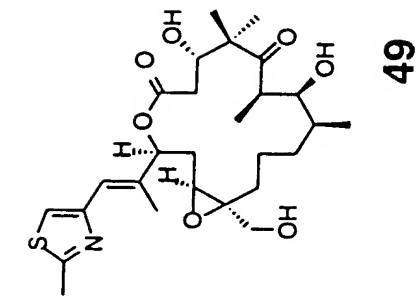


FIG. 42D



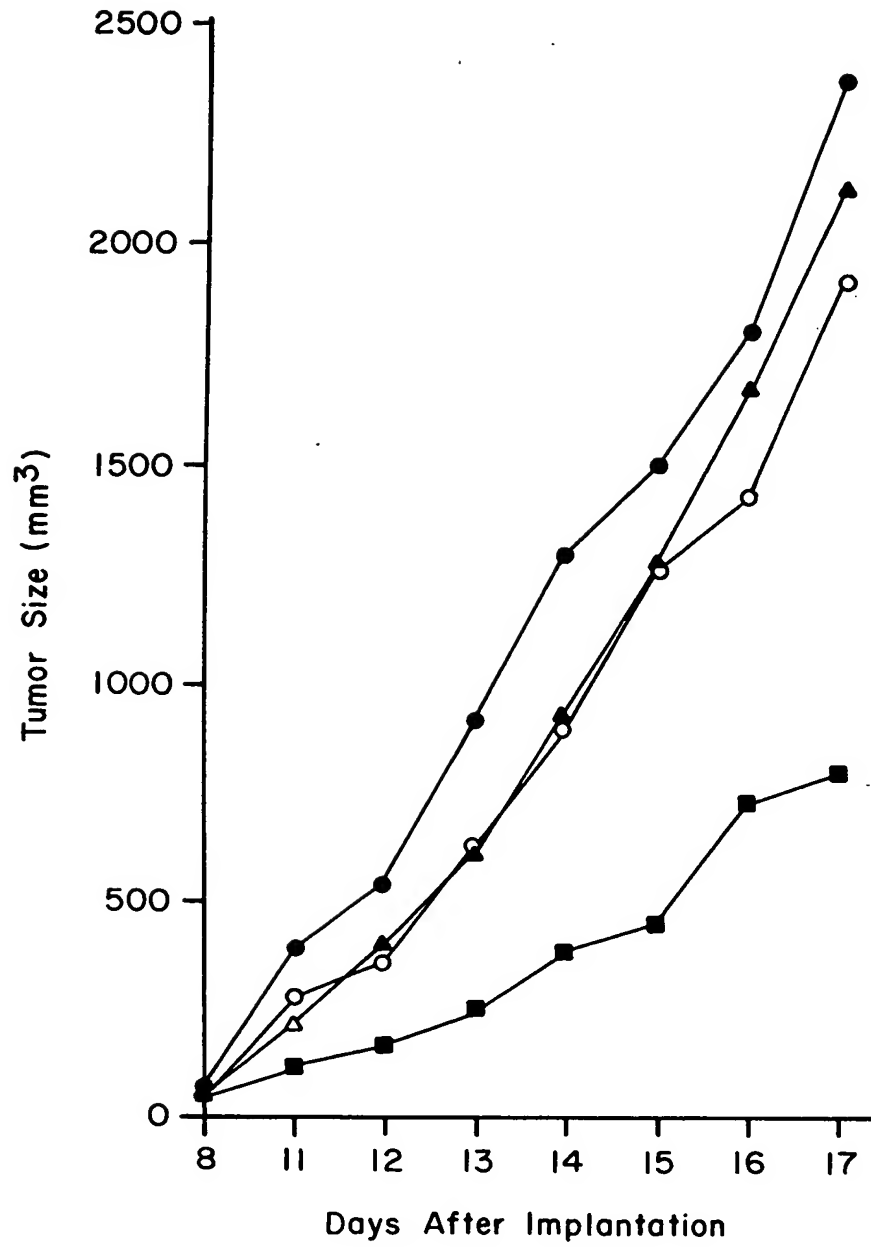
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FIG. 42E



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FIG. 43 A



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FIG. 43 B

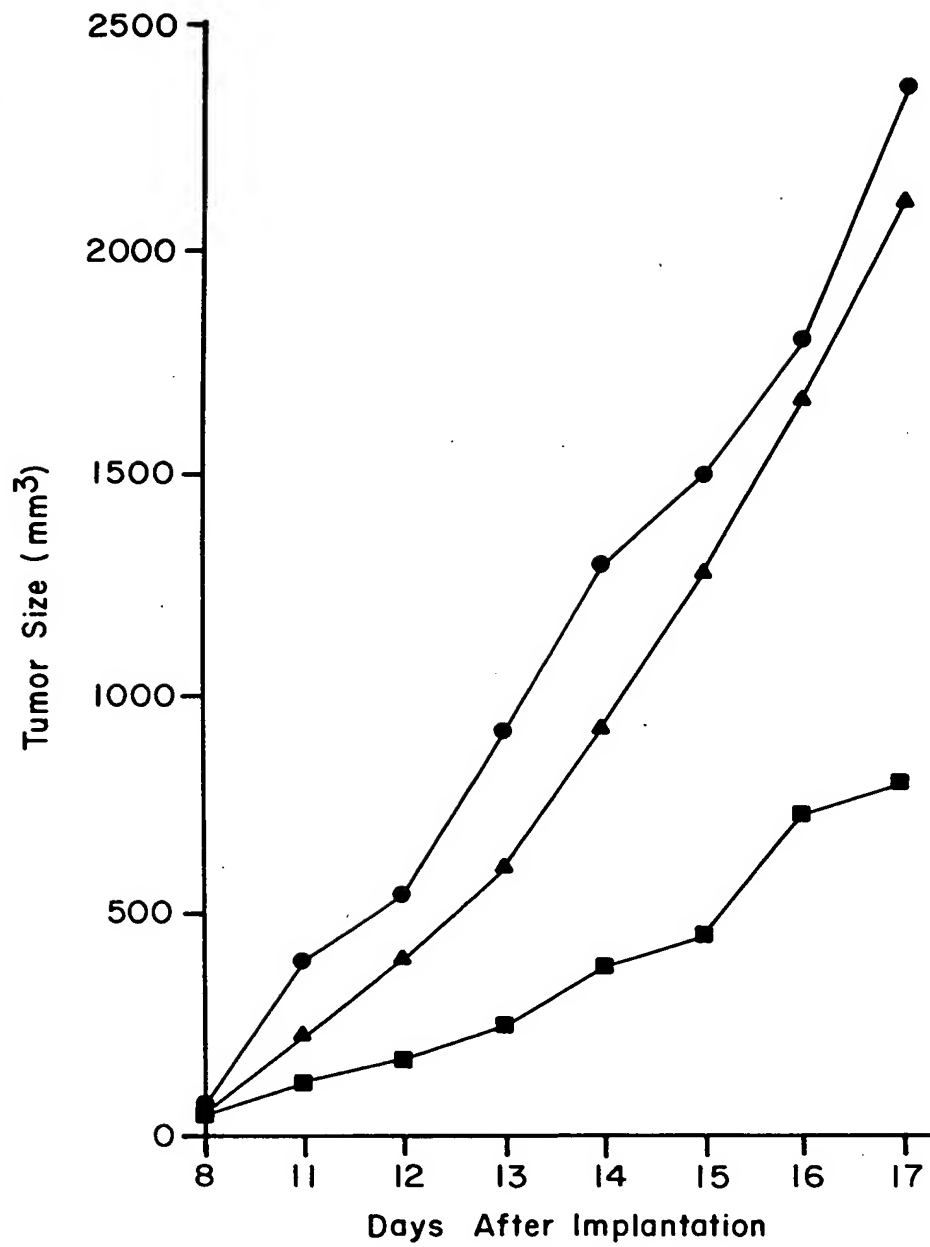
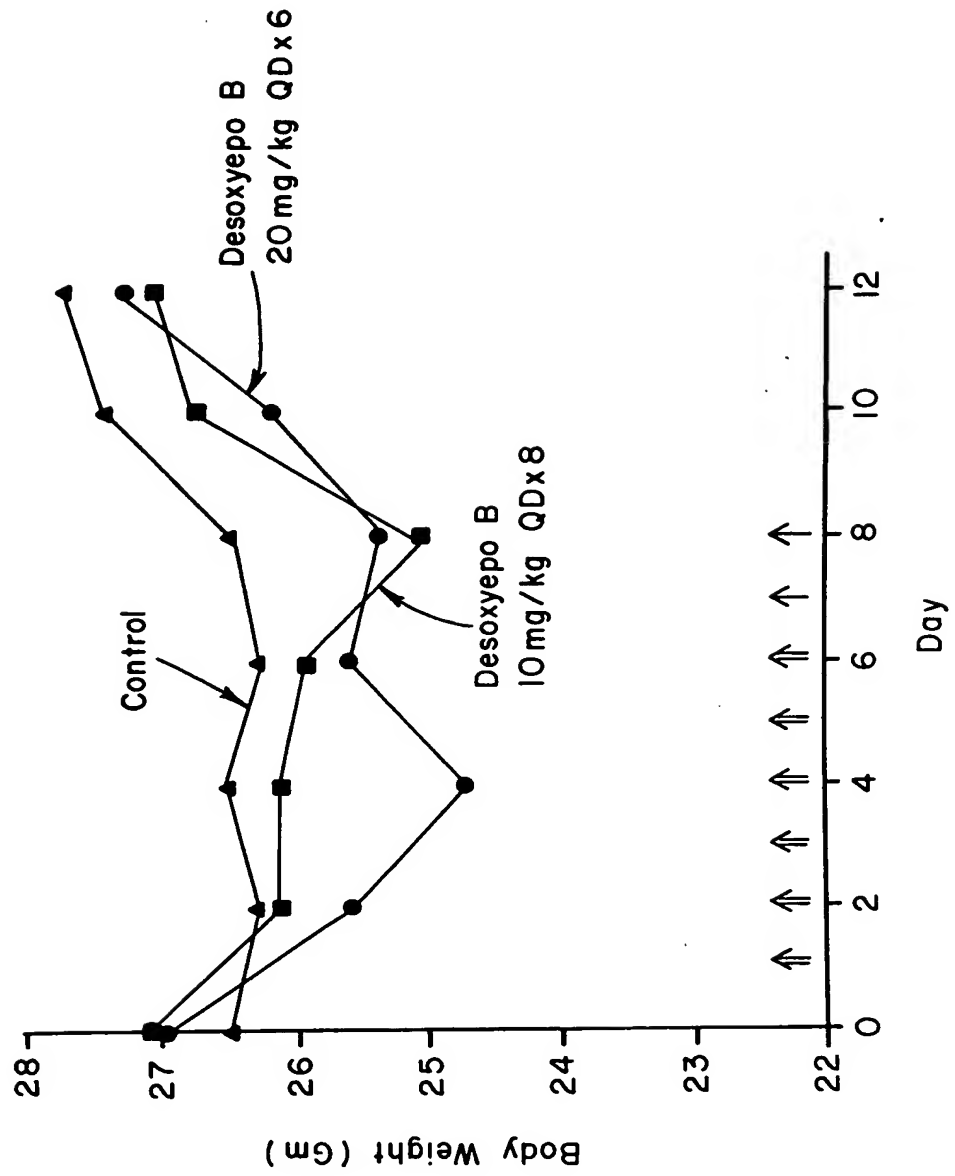
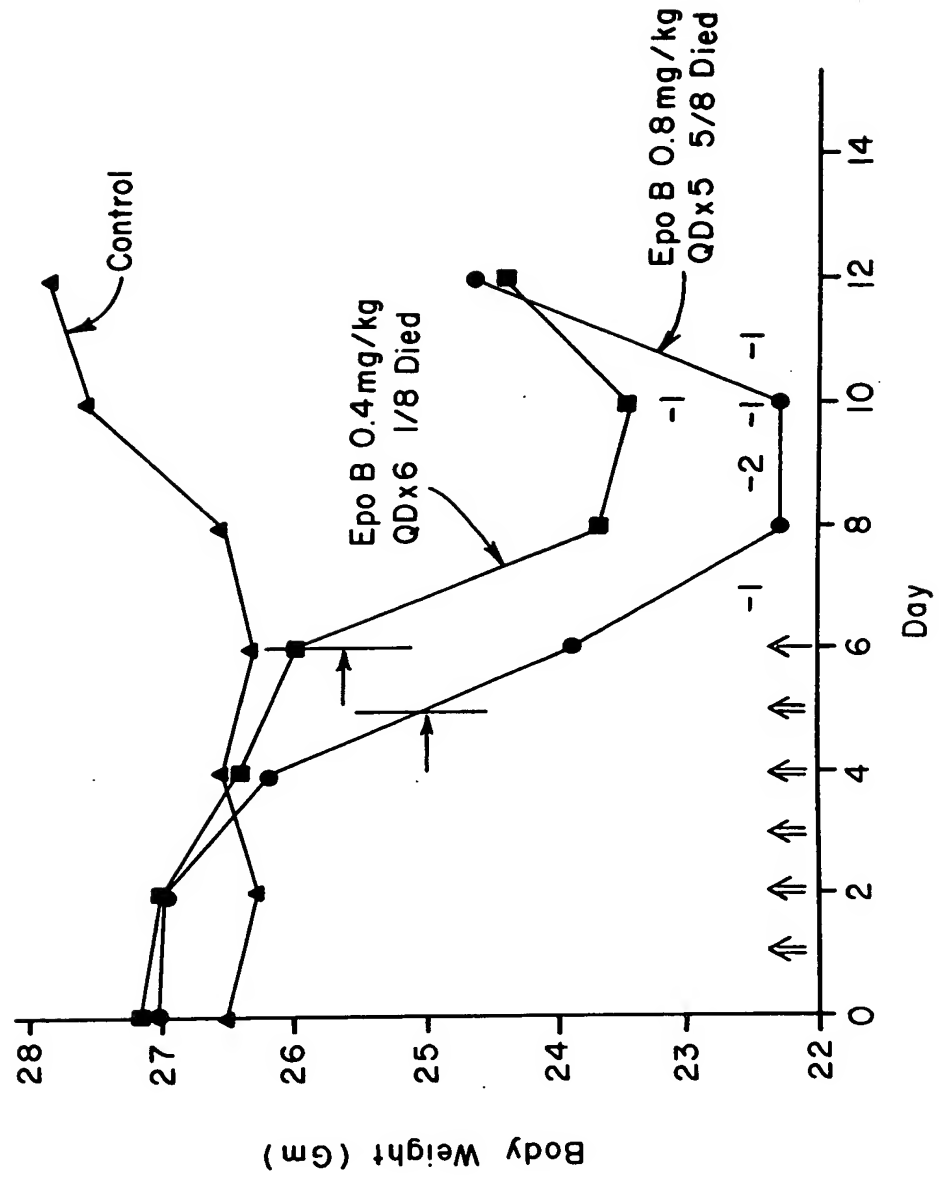


FIG. 44A



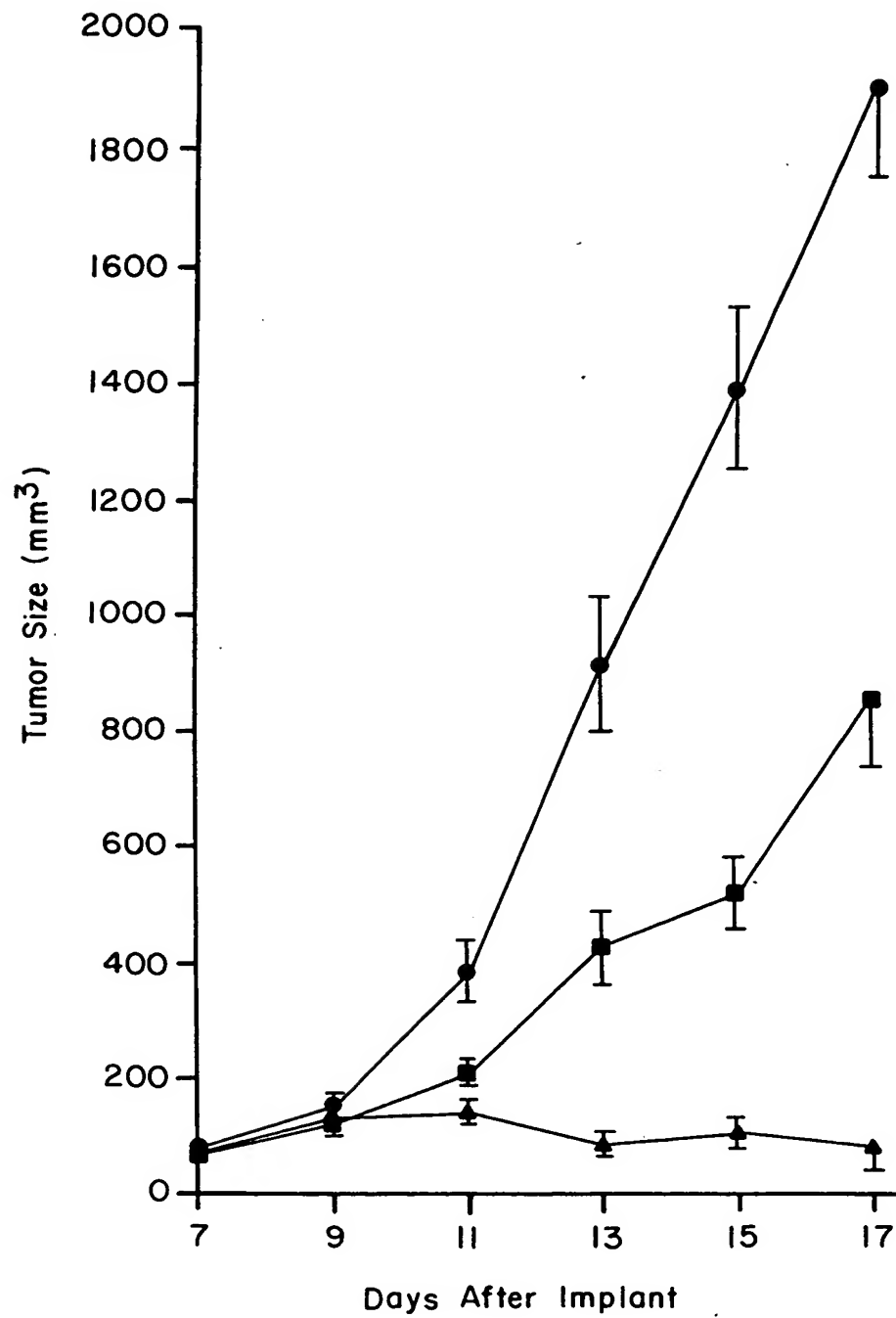
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FIG. 44B



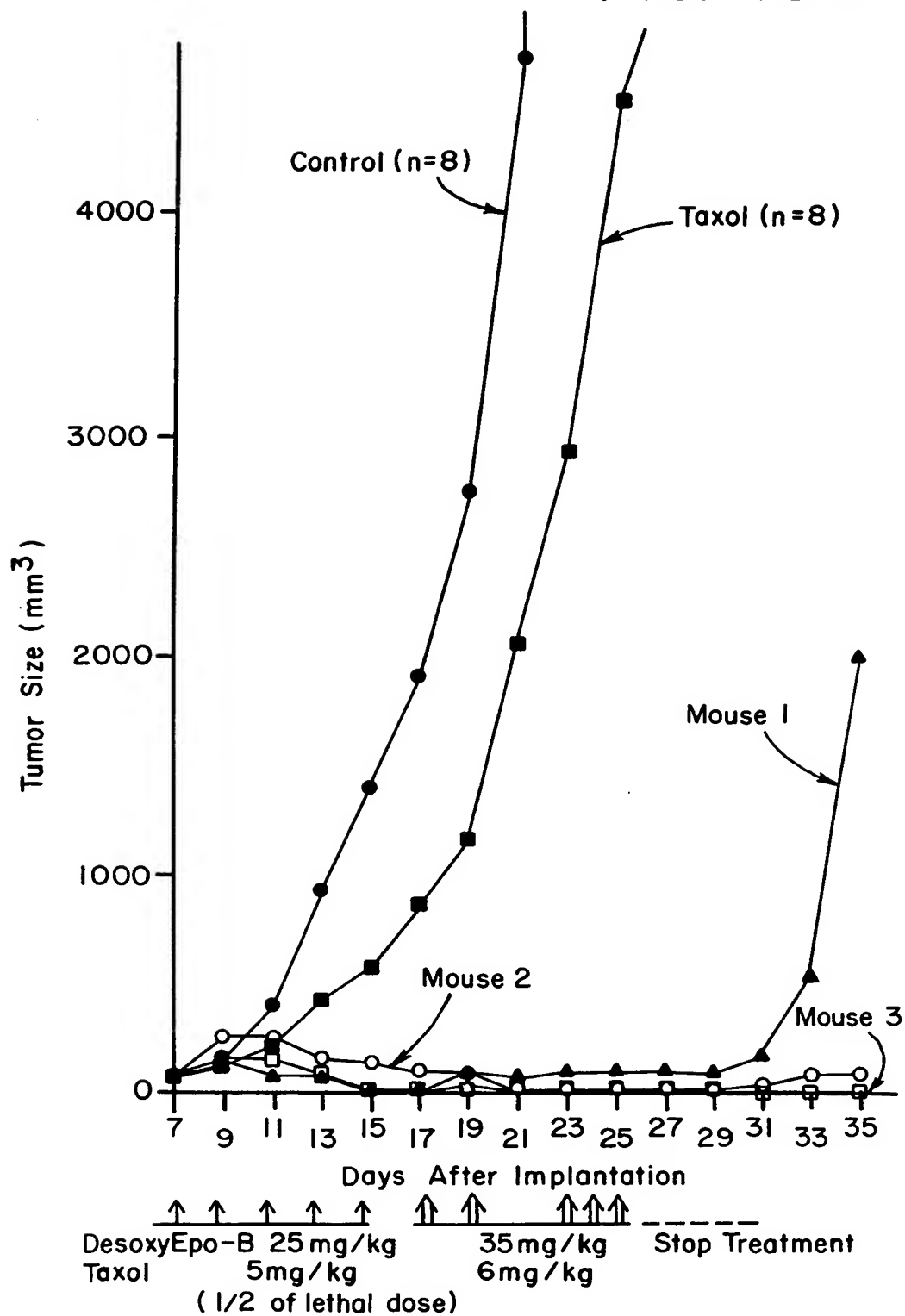
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FIG. 45A



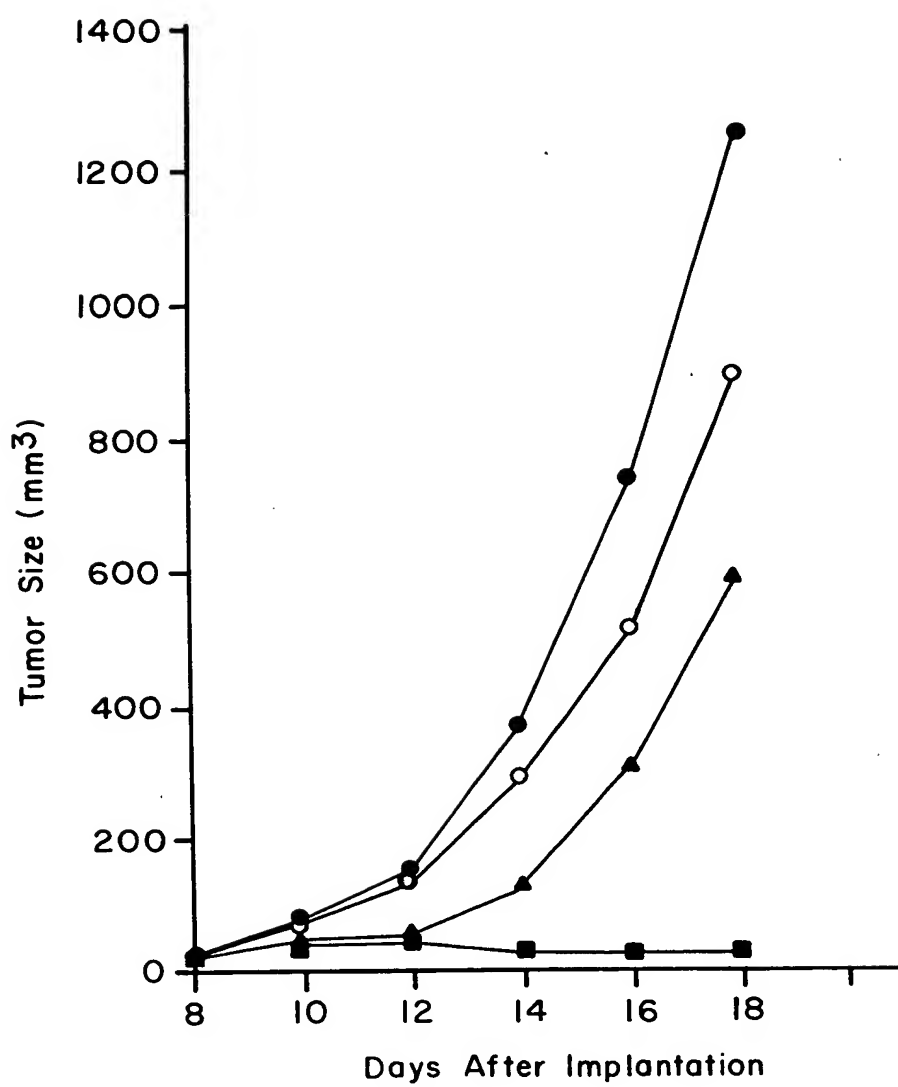
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FIG. 45 B



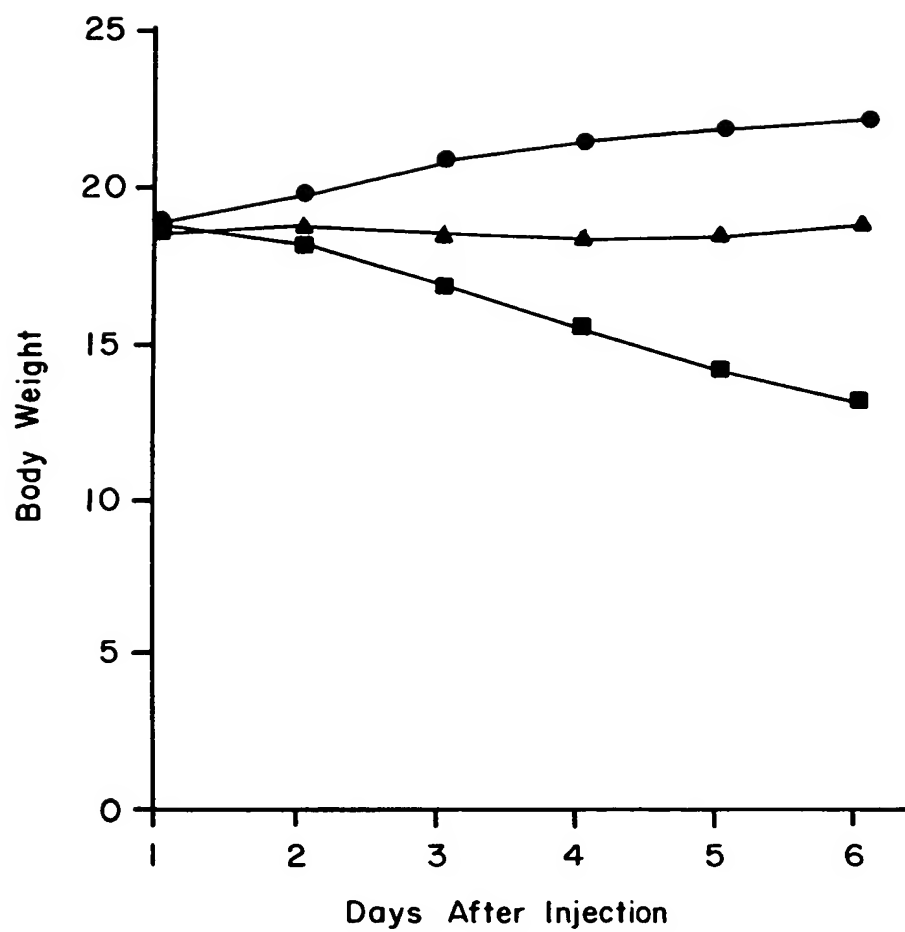
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FIG. 46



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FIG. 47



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FIG. 48

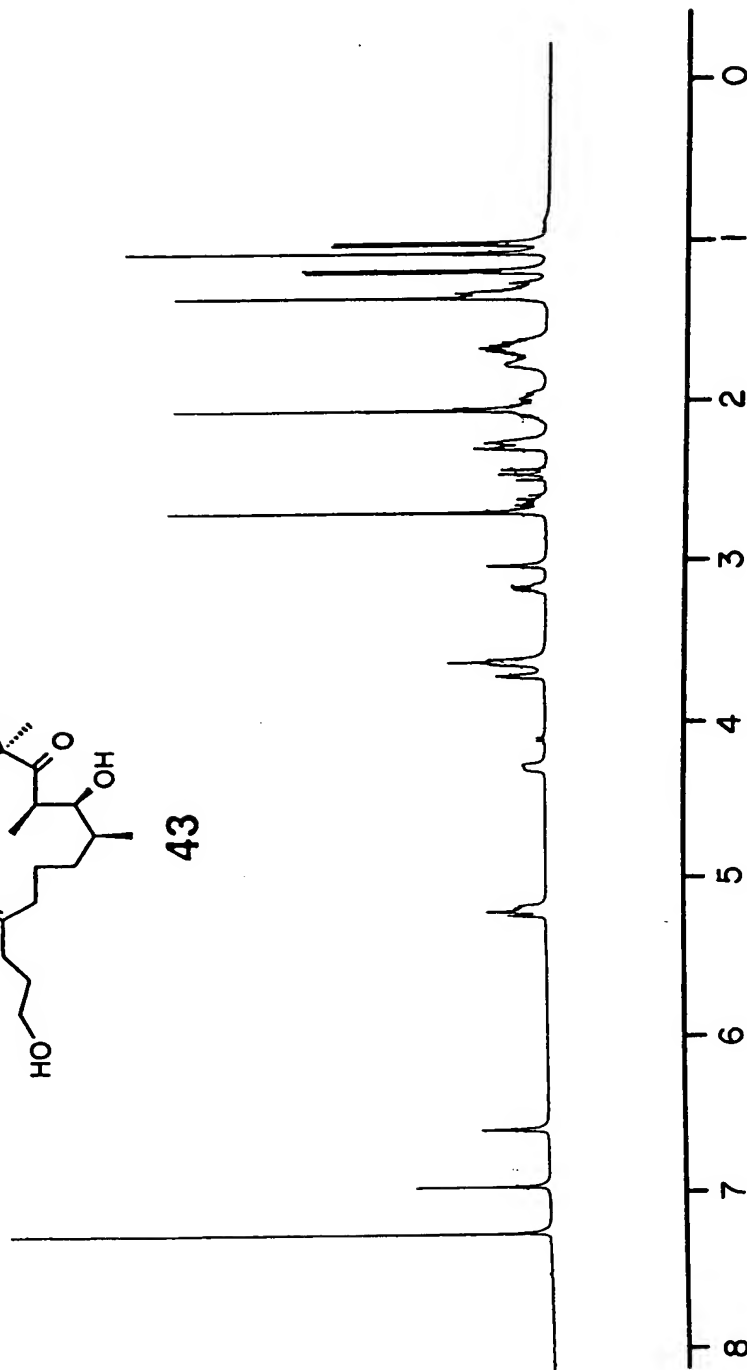
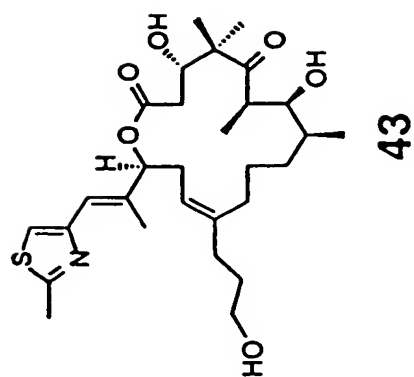
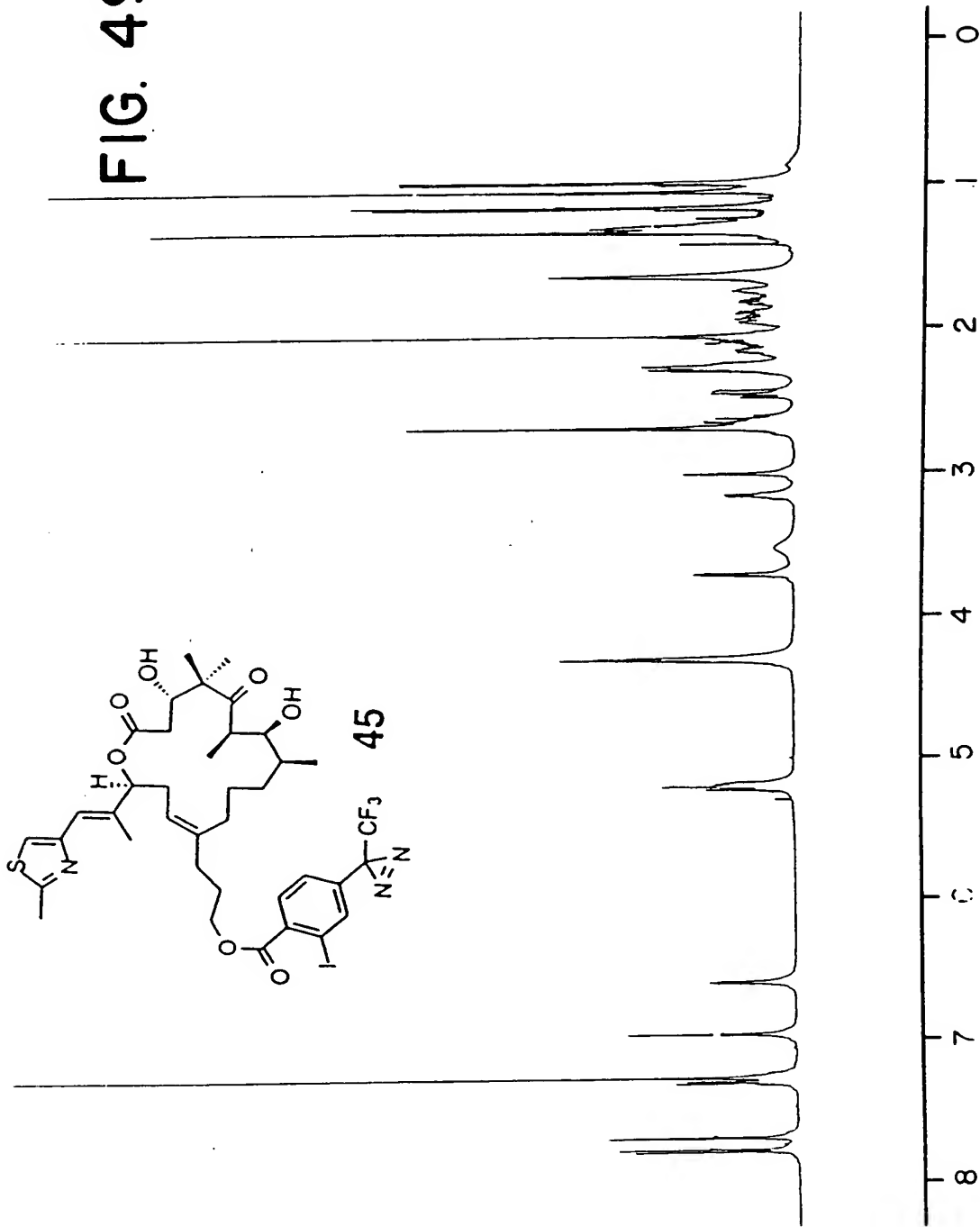
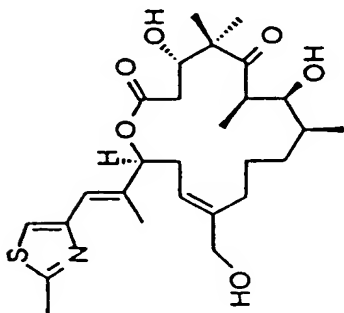


FIG. 49



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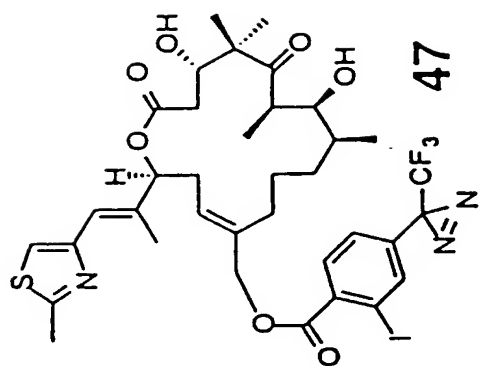


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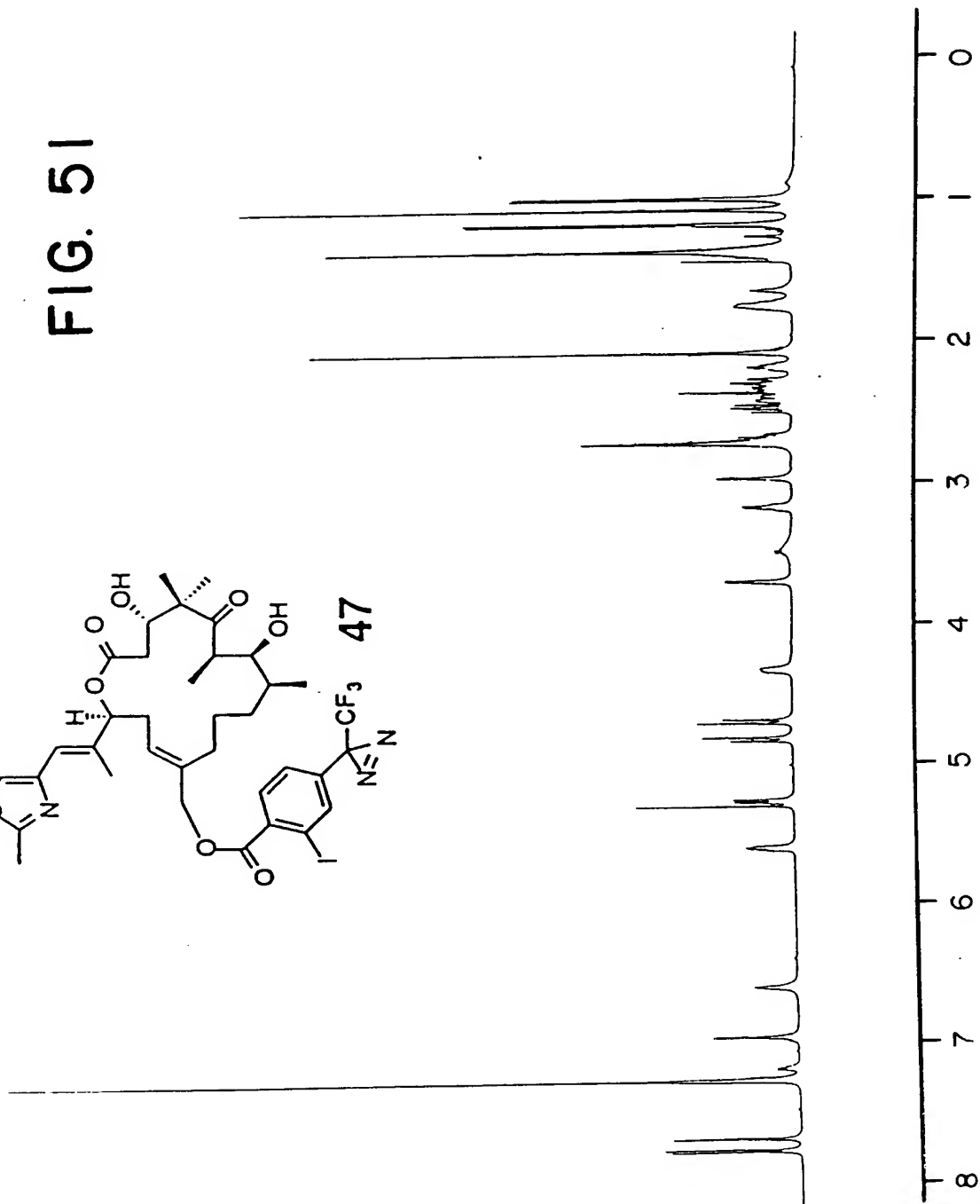
FIG. 50

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FIG. 51



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48 $R = (CH_2)_3OH$

